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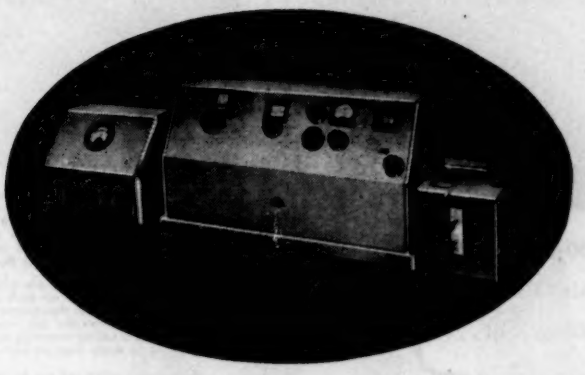

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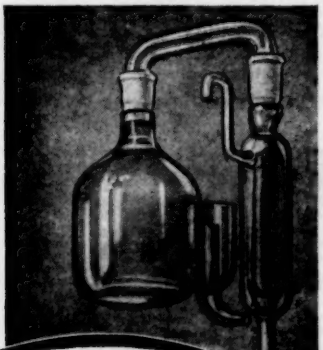

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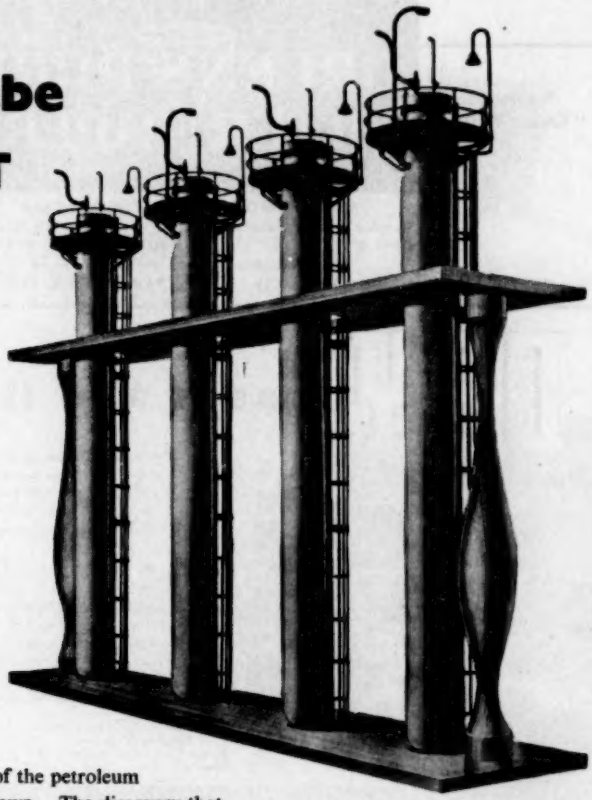

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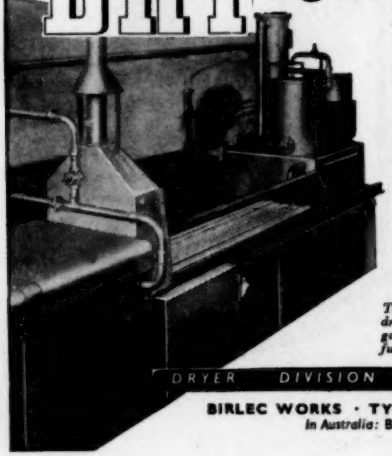

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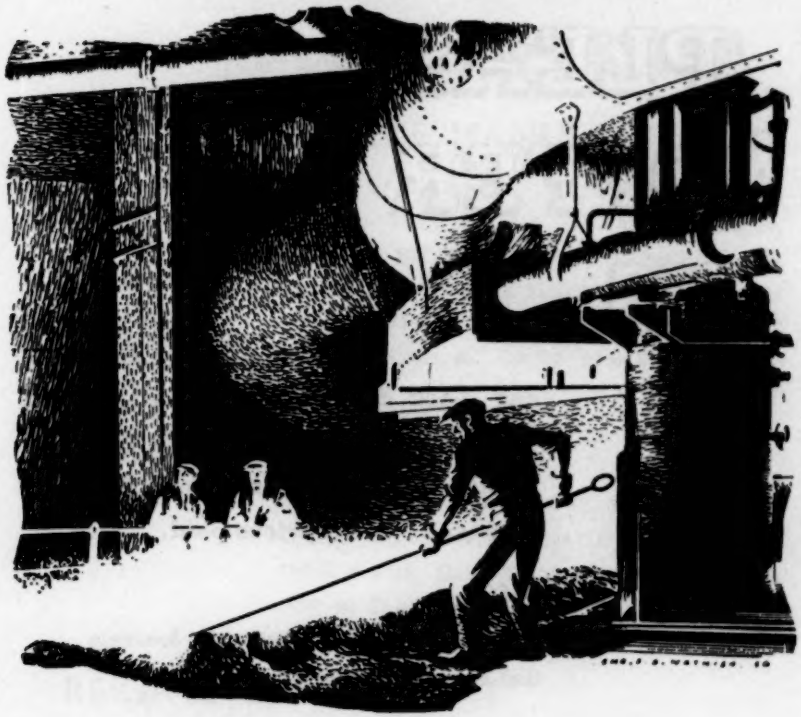

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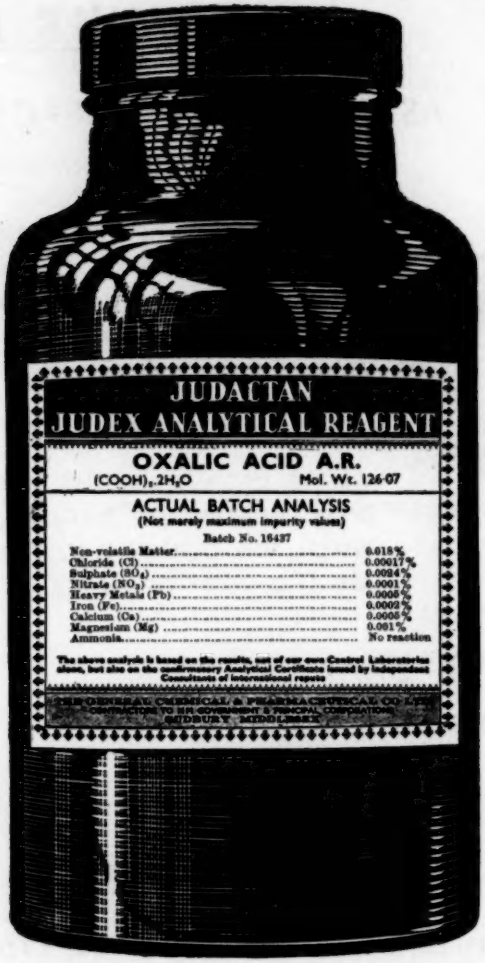

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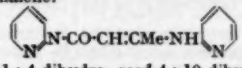
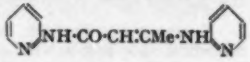
1939	1664	9 *	*for* 1936 *read* 1926.
1941	617	7 *	*for* soluble *read* insoluble.
1949	1886	11, 14 }	for N-*Methyltoluene*-p-*sulphonamide* read N-*Nitro*-N-*methyltoluene*-p-*sulphonamide*.
	3193	7 *, 8 * }	for *cresyl* read *tolyl*.
1950	318	3	*for* **61** *read* **71**.
		14 *	*for* the disulphone *read* 2 : 4-dinitrophenyl methyl sulphone.
	424	4	*for* $-1{\cdot}7 \cos \phi$ *read* $-1{\cdot}7 \cos 3\phi$.
		6 *	*for* O-outside *read* O-inside.
	426	22	*for* α-keto-carboxylic acids *read* β-keto-carboxylic acids.
		25	*for* camphoronic acid *read* camphenonic acid.
	1911	39	*for* glycollaldehyde phenylhydrazone *read* ethyl glyoxylate phenylhydrazone.
	1988	22 *	for cyclo*hexyl-β-*D-*maltose* read cyclo*hexyl-β-*D-*maltoside*.
	2208	last	*for* m. p. 270—280° *read* m. p. 279—280°.
	2210	1	*for* found *read* formed.
	3058	Table I, column 1,	*for* Epichlorohydrin *read* Glycidol.
	3172	4	*for* convenient *read* not convenient.
	3178	4 *	*for* $^{14}CH_3{\cdot}COCl$ chloride *read* $^{14}CH_3{\cdot}COCl$.
	3256	22	*for* 4 : 7-dichloro-4-hydroxy-3-phenyl-quinoline *read* 4 : 7-dichloro-3-phenyl-quinoline.
	3515	13 *, 2 * }	*for* $C_{21}H_{20}O_4N_2Cl$ *read* $C_{21}H_{19}O_4N_2ClS$.
	3607	19 *	*for* carbonate *read* sodium hydroxide; *after* (*ca.* 2·2 g.) *add*, hydrolysis of the ester having occurred in the cold.
	3641	5	*for* (XII) *read* (XIII).
	3671	page title, for *Benzine* read *Benzene*.	
1951	180	18 *	*for* $\lambda_{max.}$ 388 mμ., $\varepsilon_{max.}$ 27,000 *read* $\lambda_{max.}$ 395 mμ., $\varepsilon_{max.}$ 27,500.
	294	footnote	*for* both nitrogen atoms are *read* the nitrogen atom is.
	507	18 *, 16 * }	*for* heat of combustion *read* heat of formation.
	551	5 *	*for* 1 : 2 : 3 : 4-tetrahydro-2-keto-4-methyl 1 : 10-diazanaphthalene *read* 1 : 2 : 3 : 4-tetrahydro-4-hydroxy-2-keto-4-methyl-1 : 10-diazanaphthalene.
	552		*for*  *read* 
	552	11 *	*for* 1 : 4-dihydro- *read* 4 : 10-dihydro-.
		10 *	*for* -1 : 4-diazanaphthalene *read* -4 : 10-diazanaphthalene.
	553	14	*for* 6-chloro-, 6-amino-, *read* 7-chloro-, 7-amino-,.
		15	*for* 6-carbethoxy-, and 6-ethoxy- *read* 7-carbethoxy-, and 7-ethoxy-.
	554	15	for 1 : 4-*Dihydro*- read 4 : 10-*Dihydro*-.
	640	last	the sentence *Each reacting . . . ml.* should follow the caption to Fig. 2(*a*).
	666	15 *	*for* (VII; R = H = CHO) *read* (VII; R = H or CHO).
	714		*formula* (IIa) *should read*
	772	5 *	*for* sheet II *read* sheet I.
	773	33	*after* Mn *insert* Cu.
	774	32	*for* is not *read* is.
	812	14	*for* *p*-tolyl *read* *p*-tolyloxy.
	867	paper title,	*for* 1 : 2 : 3 : 4 : 9 : 10- *read* 1 : 2 : 3 : 8 : 9 : 10-.
	1143	summary, line 4,	*for* γ-methyl *read* methyl.
		summary, line 5,	*for* (I) *read* (I; R = Me).

* From bottom of page.

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316. *The Oxidation of Toluene by Sodium Dichromate.*

By Robert D. Abell.

Oxidation of toluene by sodium dichromate and sulphuric acid gives, besides benzoic acid and benzaldehyde, mainly phenyl *o*-, *m*-, and *p*-tolyl ketone and phenyl-*o*-, -*m*-, and -*p*-tolylmethane (these two sets of products in the ratio 2 : 1), and very small amounts of benzyl alcohol, dibenzyl, diphenylmethane, and anthraquinone.

This paper records an investigation of the products, other than acids, formed when toluene is oxidised by sodium dichromate and sulphuric acid. The general procedure was to use a relatively small amount of oxidising agent so that the excess of toluene acted as solvent for the oxidation products, then to remove the aqueous layer, extract the organic acids with aqueous alkali, and to submit the organic layer to further oxidation after it had been made up to its original volume with more toluene. In this way a toluene solution containing 35—40% of neutral oxidation products was obtained.

The neutral products were found to consist mainly of phenyl *o*-, *m*-, and *p*-tolyl ketones, phenyl-*o*-, -*m*-, and -*p*-tolylmethanes, benzyl alcohol, benzaldehyde, a very small amount of dibenzyl, and traces of diphenylmethane and anthraquinone. Of these, the three ketones and phenyl-*m*-tolylmethane appear not to have been recorded previously among the oxidation products of toluene (cf. Beilstein, "Handbuch der Organischen Chemie," 4th edn., Vol. V, p. 284). After removal of benzyl alcohol, benzaldehyde, and benzoic acid, fractionation of the crude product between light petroleum and sulphuric acid separates the hydrocarbons from the ketones and gives the following composition: ketones 60%; hydrocarbons 30%; unidentified substances 10% (of which 6% is separable as being soluble in ether but insoluble in light petroleum).

Substantial amounts of phenyl *p*-tolyl ketone are readily obtained crystalline. The other ketones were obtained as mixtures of isomers; they were identified by analysis of the mixture and by its oxidation to benzoylbenzoic acids which were separated and identified. The diarylmethanes were also obtained as mixed isomers, which were recognised by analysis and oxidation to the mixed ketones (from which some of the *p*-compound was obtained crystalline) and then to the benzoylbenzoic acids which were again separated and identified.

It seems probable that the diphenylmethane owes its origin to a little benzene present in the commercial toluene used.

Experimental.

(Light petroleum used in this work had b. p. 40—60°.)

The starting material was produced in a commercial process for the preparation of benzoic acid by oxidation of toluene by aqueous sodium dichromate and sulphuric acid in a 2000-gallon lead-lined vat, with vigorous stirring. When all the dichromate had been reduced, the aqueous layer was run off, and the organic layer extracted with sodium hydroxide solution, which was then heated, acidified with hydrochloric acid, cooled, and filtered. The precipitate was washed until acid-free, dried, sublimed, and identified as benzoic acid (m. p. and mixed m. p. 121°). The residual toluene solution was made up to its original volume with more toluene and again treated as above, this process being repeated until the toluene contained *ca.* 40% of oxidation products. 1·5 Gallons of this solution were worked up as recorded below with overall loss of only a few grams.

Initial Fractionation.—(*a*) Most of the unchanged toluene was removed by distillation and the resulting "toluene residues" were treated by one of the following procedures.

(i) The residues were distilled in steam from a bath at 100—110°, benzyl alcohol, benzaldehyde, and a small amount of anthraquinone being thus removed as well as residual benzoic acid. Distillation in superheated steam, from a bath at 250°, then gave a clear yellow oil and a dark friable residue (*ca.* 4%). The former was dried ($CaCl_2$) and fractionated *in vacuo* [see (*b*) below].

(ii) Alternatively, the "toluene residues" were distilled in steam as above at 100—110°, and the involatile material dried and directly fractionated *in vacuo* as in (*b*) below.

(iii) In a third method, the "toluene residues" were diluted with toluene, ether, or light petroleum, extracted successively with aqueous sodium hydroxide, aqueous sodium hydrogen sulphite (which removed benzaldehyde), aqueous sodium hydroxide, and water, and dried ($CaCl_2$), filtered, and fractionated as in (*b*) below.

(*b*) The yellow oil from (i) or the residue from (ii) or (iii) above was fractionally distilled (b. p. range 90—195°/18 mm.); fractions of b. p. 180—187°/18 mm. and 187—195°/18 mm. partly solidified, the former only on cooling, to yield phenyl *p*-tolyl ketone (see below), m. p. 54°, which was removed. Repeated fractional distillation concentrated the material into a fraction (*A*), b. p. 143—145°/10 mm. and a portion (*B*), b. p. 165—185°/10 mm., with small intermediate fractions of intermediate composition. The difference in b. p.s permitted almost complete separation of fractions (*A*) and (*B*). These fractions

could, however, not be satisfactorily sub-divided, although partial concentration of the *p*-ketone was effected. Substantial amounts of crystalline phenyl *p*-tolyl ketone, obtained from various fractions, particularly those of higher b. p., were separated as far as possible, and identified (see below).

Fraction (A). *Diarylmethanes.*—This purely hydrocarbon fraction (Found: C, 92·0; H, 8·0%) consisted mainly of phenyltolylmethanes (Calc. for $C_{14}H_{14}$: C, 92·3; H, 7·7%), but analysis does not exclude the presence of the isomeric dibenzyl, and an orange-like odour indicated the presence of some diphenylmethane. Treatment of fraction (*A*) (50 g.) with chromium trioxide (40 g., equiv. to *ca.* 2·2 atoms of O) gave neutral products (*C*) (46·5 g.), that had lost the orange-like odour, and a very small quantity of acids (benzoic, which arises from dibenzyl, with a little *o*-benzoylbenzoic acid). Oxidation of fraction (*A*) (50 g.) with potassium permanganate (65 g., equiv. to *ca.* 2·2 atoms of O) gave neutral products (*C'*) (50 g.) and a similar mixture of acids (3·5 g.). As under these conditions phenyltolylmethanes give ketones and only traces of benzoylbenzoic acids, dibenzyl gives benzoic acid, and diphenylmethane gives benzophenone, the results of the above oxidations indicate that fraction (*A*) contained very approximately 5% of dibenzyl and 2% of diphenylmethane (which was responsible for the orange-like odour).

From its analysis (Found: C, 85·9, 86·0; H, 7·2, 7·1%) the oil (*C* or *C'*) seemed to contain phenyl tolyl ketones (Calc. for $C_{14}H_{12}O$: C, 85·7; H, 6·1%) and some unchanged hydrocarbon. In agreement therewith it boiled over a range (mainly 145—175°/10 mm.). Fractions obtained in such distillations yielded, on oxidation with chromium trioxide, mixed benzoylbenzoic acids in which the *o*-acid predominated.

The Portion (B). *Diaryl Ketones.*—That the fraction of b. p. 165—168°/10 mm. is composed of phenyl tolyl ketones is indicated by analysis before (Found: C, 85·4; H, 6·4%) and after (Found: C, 85·5; H, 6·4%) the usual oxidation procedure. Treatment of this fraction of the material (*B*) (20 g.) with chromium trioxide (40 g.) in boiling acetic acid (150 c.c.) for 120 hours gave 10 g. of (mainly *o*-) benzoylbenzoic acid and 4 g. of unchanged ketone. Similarly, from 20 g. of the same fraction (*B*) potassium permanganate (32 g.) in water (1 l.) gave, after 2 months at room temperature, 10·0 g. of unchanged ketone, 9 g. of the three benzoylbenzoic acids, and a small amount of benzoic acid.

Two fractions contiguous to the above-mentioned fraction contained substantially only phenyl tolyl ketones [Found (fraction of b. p. 168—172°/10 mm.): C, 85·5; H, 6·3; (fraction of b. p. 172—180°/10 mm.): C, 85·5; H, 6·4%]. Each was oxidised by chromium trioxide or potassium permanganate, giving the three benzoylbenzoic acids; the highest-boiling fraction gave the largest proportion of *p*-isomer.

Other Fractions.—Three small fractions, intermediate between (*A*) and (*B*) and boiling between 145° and 160° at 10 mm., were united (total, 23 g.) and heated with chromium trioxide (23 g.) in acetic acid (100 c.c.) for 9 hours, yielding mainly ketones (19·5 g.) with only 1 g. of benzoylbenzoic acids (*o*- and *p*-isomers identified). These fractions thus contained mainly phenyltolylmethanes.

A fourth and larger intermediate fraction, b. p. 160—165°/10 mm., contained a large proportion of phenyl-*o*-tolylmethane, for on prolonged oxidation (30 g. of fraction; 75 g. of chromium trioxide in 200 c.c. of acetic acid; 100 hours' boiling) it afforded 2·5 g. of neutral material and 29·5 g. of the three benzoylbenzoic acids in which the *o*-isomer predominated

Distillation Residues.—A residue was obtained at each distillation. Each was extracted with light petroleum which removed an oil which was added to another appropriate fraction. Treatment of the remainder with ether yielded, usually, a small amount of anthraquinone (m. p. and mixed m. p. 273°) and, in all cases, a high-boiling oil, of which altogether 52 g. were accumulated. This oil (52 g.) was boiled with chromium trioxide (40 g.) in acetic acid, giving a brown amorphous acid (3·6 g.) but no benzoylbenzoic acid, so that none of the phenyl tolyl ketones was present; much (30 g.) of the oil was recovered after the oxidation.

Phenyl p-*Tolyl Ketone.*—This ketone was identified by its m. p. and mixed m. p. (both 54°), by analysis (Found: C, 85·55; H, 6·2%), and by oxidation by chromium trioxide to *p*-benzoylbenzoic acid only (m. p. and mixed m. p. 193—194°).

Separation of Benzoylbenzoic Acids.—Separation of the acids formed on oxidation was always tedious and varied somewhat according to the composition of the mixture under examination. The following is a typical example. It should be added that no fraction was neglected and that acids other than benzoic and the benzoylbenzoic acids were definitely absent.

The mixed acids (10—15 g.) were shaken with successive amounts (each 600 c.c.) of water at 80—85° to give saturated solutions which were then filtered. Gradual separation occurred, to yield first *p*-benzoylbenzoic acid as the least soluble portion, m. p. 175—190°, which crystallised from methyl alcohol in plates, m. p. 194° alone or mixed with an authentic specimen (Found: C, 74·25; H, 4·3. Calc. for $C_{14}H_{10}O_3$: C, 74·3; H, 4·4%). The aqueous filtrates, on slow cooling, deposited (*a*) woolly flocks, m. p. 140—145°, (*b*) large transparent flattened prisms, m. p. 90—94°, and (*c*) globules of oil which crystallised when cold. The flocks were separated by decantation, and the solidified globules by hand-picking. The cold filtrates from these three materials deposited during 2 days small glistening prisms, identified by their m. p. and mixed m. p. (both 93—94°) as *o*-benzoylbenzoic acid hydrate. The woolly flocks (*a*) and the large prisms (*b*) were further fractionally crystallised from water until only one type of crystal was obtained in each fraction.

On extraction of the flocks with carbon disulphide there remained *m*-benzoylbenzoic acid as small glistening needles, m. p. and mixed m. p. 160—161° (Found: C, 74·2; H, 4·5%). When the prisms (*b*) were extracted with cold carbon disulphide there remained *o*-benzoylbenzoic acid hydrate, m. p. and mixed m. p. 93—94° (Found: C, 68·6; H, 5·1. Calc. for $C_{14}H_{10}O_3,H_2O$: C, 68·8; H, 5·0%), which at 100—115° afforded the anhydrous acid, m. p. and mixed m. p. 126—127°. The solidified globules (*c*), when ground and extracted with cold carbon disulphide, gave the insoluble *o*-benzoylbenzoic acid (does

not readily sublime) and the much more soluble benzoic acid (sublimes readily), m. p. and mixed m. p. 121°.

In some cases, for *o* + *p*-mixtures, the difference in the solubilities of the barium and the calcium salts in water and alcohol was also utilised for separations; in others, fractional precipitation of the acids from aqueous solutions of the sodium salts was an aid.

Over-all Composition.—0·5 Kg. of the oil remaining after the initial distillation of the crude " toluene residues " was dissolved in light petroleum (2·5 l.), kept for several days, and decanted from a small amount of dark sludge (5 g.). The solution was then shaken cautiously with successive portions (150, 100, and 50 c.c.) of concentrated sulphuric acid; the third extraction removed little, for no heat was generated and the acid became green and not brown

The petroleum solution, now much lighter, was washed free from acid, dried, and evaporated, giving a pale oil (145 g.), which afforded fractions of b. p. 140—150° (mainly 143—145°)/10 mm. (120 g.) and 150—160°/10 mm. (25 g.) and a small, dark, foul-smelling residue. The b. p.s and oxidation to the benzoylbenzoic and benzoic acids indicate the composition as diarylmethanes (plus dibenzyl).

The sulphuric acid solution was poured into water (2 l.) and shaken with a large volume of light petroleum. The whole was filtered through a fluted paper which retained a dark viscid oil (30 g.), almost completely soluble in ether. The aqueous acid was discarded. The petroleum solution gave, on evaporation, an oil (320 g.) which, when dried and distilled, gave three fractions, b. p. 160—168°/10 mm., 168—175°/10 mm., and 175—185°/10 mm., and a residue (which behaved like, and was treated as, the residues described above). The second and the third fraction partly crystallised, the third prolifically. All three fractions were cooled and filtered; the crystals, washed with light petroleum, had m. p. 54° (38·0 g.). Three repetitions of the distillation and crystallisations afforded more of this phenyl *p*-tolyl ketone, and 80·0 g. in all were collected. This isolation, the b. p.s, and oxidation to benzoylbenzoic acids show the sulphuric acid-soluble material to contain essentially only ketones.

The separations are clear-cut and lead to the over-all composition given on p. 1379.

This work was carried out at Bradford Technical College.

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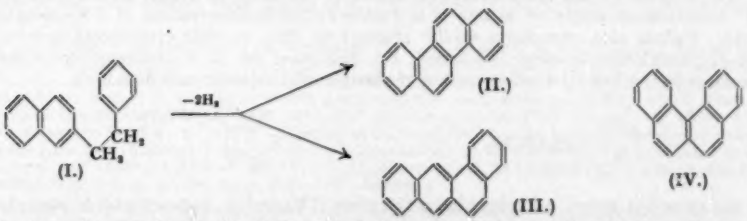
317. *The Phenanthrene Cyclisation of Dibenzyl-type Derivatives.*

By NG. PH. BUU-HOÏ, NG. HOÁN, and PIERRE JACQUIGNON.

The limitations of the aluminium chloride-catalysed cyclodehydrogenation of dibenzyl compounds to phenanthrene derivatives have been investigated in a number of instances in the benzene, thiophen, and naphthalene series; in the naphthalene series, new examples of molecular rearrangements accompanying the cyclisation have been brought to light.

RUZIČKA AND HÖSLI (*Helv. Chim. Acta*, 1934, **17**, 470) found that treatment of dibenzyl with aluminium chloride in carbon disulphide solution gave phenanthrene in 15% yield, and later Ruzička and Márkus (*ibid.*, 1940, **23**, 385) prepared 3-methylchrysene similarly from 1-methyl-5-2′-phenylethylnaphthalene. In spite of its potential practical interest for the preparation of phenanthrene derivatives and of its interesting theoretical implications, this cyclodehydrogenation reaction has not since been investigated, except for a recent synthesis of picene from 1 : 2-di-1′-naphthylethane (Buu-Hoï and Hoán, *J. Org. Chem.*, 1949, **14**, 1023).

The present work deals with a preliminary investigation of the possible use of this reaction for the preparation of phenanthrene derivatives in the aromatic and heterocyclic series. An attempt to prepare 3 : 4-benzophenanthrene (IV) by the aluminium chloride-catalysed cyclodehydrogenation of 2-2′-phenylethylnaphthalene (I) resulted in none of this hydrocarbon, but gave a mixture of chrysene (II) with some 1 : 2-benzanthracene (III) :

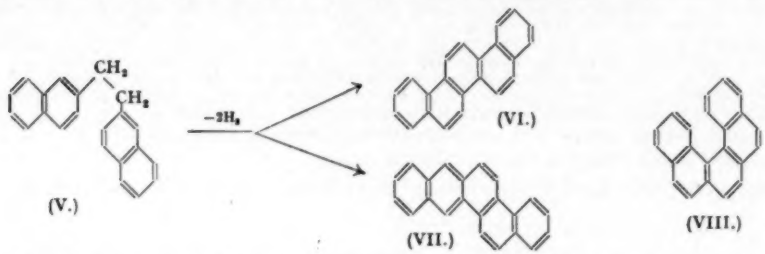


The formation of chrysene from (I) involved a shift of the substituent from the 2- to the 1-position on the naphthalene nucleus; this is a rather unusual feature, but some indications in

the literature point to the likelihood of such β ⟶ α conversions. For instance, Chattaway and Lewis (*J.*, 1894, **65**, 869) observed that β-chloronaphthalene is partly converted into the α-isomer under the influence of small amounts of aluminium chloride; in the same conditions, β-bromonaphthalene is similarly converted into the α-isomer. More recently, Wibaut, Sixma, and Suyver (*Rec. Trav. chim.*, 1949, **68**, 526) observed that rearrangement anew, and found that an equilibrium is reached under the influence of aluminium chloride, starting from either α- or β-bromonaphthalene.

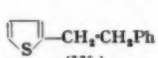
The concurrent formation of 1 : 2-benzanthracene is similar to the preferential Pschorr cyclisation of the diazo-compound from *o*-amino-α-2-naphthylcinnamic acid to 1 : 2-benzanthracene instead of to the expected 3 : 4-benzophenanthrene (Cook, *J.*, 1930, 1089; cf. Weitzenböck and Lieb, *Monatsh.*, 1912, **33**, 564).

Cyclodehydrogenation of 1 : 2-di-2′-naphthylethane (V) was also anomalous, for in place of the expected 3 : 4-5 : 6-dibenzophenanthrene (VIII), we obtained a mixture of picene (VI) with some naphtho(2′ : 1′-1 : 2)anthracene (1 : 2-6 : 7-dibenzophenanthrene) (VII) :

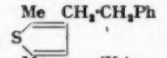


2-2′-Phenylethylnaphthalene was prepared by Wolff–Kishner–Huang-Minlon reduction (*J. Amer. Chem. Soc.*, 1946, **68**, 2847) of 2-phenylacetylnaphthalene, which we obtained most easily by a Friedel–Crafts reaction between phenylacetyl chloride and naphthalene in nitrobenzene (cf. Buu-Hoï and Cagniant, *Bull. Soc. chim.*, 1945, **12**, 307). This was a marked improvement in the preparation of that ketone by the earlier procedures which necessitated a separation of the two isomers through their picrates (see, for instance, Ruggli and Reinert, *Helv. Chim. Acta*, 1926, **9**, 71). Similarly, 6-methyl-2- and 1-methyl-7-2′-phenylethylnaphthalene and 1-methyl-4-2′-phenylethylnaphthalene were prepared from the corresponding ketones (Buu-Hoï and Royer, *Rec. Trav. chim.*, 1946, **65**, 251; Cook and Galley, *J.*, 1931, 2012). In the case of 2 : 3-dimethylnaphthalene, phenylacetylation in nitrobenzene yielded a homogeneous ketone which should be 2 : 3-dimethyl-6-phenylacetylnaphthalene in view of the results of the Friedel–Crafts condensation of this hydrocarbon with succinic (Haworth and Bolam, *J.*, 1932, 2248) and phthalic anhydrides (Fieser and Fieser, *J. Amer. Chem. Soc.*, 1933, **55**, 3342; Fieser and Peters, *ibid.*, 1932, **54**, 3742). In agreement with this constitution was the Pfitzinger condensation with isatin to give the corresponding cinchoninic acid in high yield, a proof that no methyl group was present *ortho* to the carbonyl group (cf. Buu-Hoï *et al.*, *Bull. Soc. chim.*, 1946, **13**, 123, 134, 374). Wolff–Kishner–Huang-Minlon reduction of this ketone gave 2 : 3-dimethyl-6-2′-phenylethylnaphthalene (3-2′-phenylethylpyrene could similarly be obtained from 3-phenylacetylpyrene). Treated with aluminium chloride, the above naphthalene hydrocarbons yielded very impure cyclodehydrogenation products.

In the benzene group, an unsuccessful attempt was made to synthesise either picene or 1 : 2-5 : 6-dibenzanthracene by means of a double cyclodehydrogenation of 4-2′-phenylethyldibenzyl. Failure also attended a similar attempt to effect a triple cyclodehydrogenation of 4 : 4′-di-(2-phenylethyl)dibenzyl (obtained by reduction of 4 : 4′-bisphenylacetyldibenzyl, a by-product in the Friedel–Crafts reaction of phenylacetyl chloride with dibenzyl).



(IX.)



(X.)

In the thiophen series, 2-2′-phenylethylthiophen (IX) and 2 : 5-dimethyl-3-2′-phenylethylthiophen (X) were largely decomposed when heated with aluminium chloride in carbon disulphide.

Experimental.

2-Phenylacetylnaphthalene.—To a well-stirred, ice-cooled solution of phenylacetyl chloride (50 g.) and naphthalene (50 g.) in nitrobenzene (200 c.c.), powdered aluminium chloride (50 g.) was added in small portions. The mixture was kept overnight at room temperature, then poured on cracked ice, the nitrobenzene removed by steam-distillation, and the residue taken up in benzene. After drying (Na_2SO_4) and removal of the solvent, the residue was distilled *in vacuo*, to give 2-phenylacetylnaphthalene, b. p. *ca.* 238°/16 mm., crystallising from ethanol in prisms (25 g.), m. p. 100°. Ruggli and Reinert (*loc. cit.*) gave m. p. 99—99·5°.

2-2′-Phenylethylnaphthalene.—A mixture of pure 2-phenylacetylnaphthalene (22 g.), 85% hydrazine hydrate (22 g.), potassium hydroxide (22 g.), and diethylene glycol (125 c.c.) was gradually heated to 200° with removal of water, and then refluxed for 2 hours. After cooling, the reaction mixture was diluted with water, and the hydrocarbon formed taken up in benzene. The benzene solution was washed with dilute hydrochloric acid, then with water, and dried (Na_2SO_4). After removal of the solvent, the residue gave, on vacuum-distillation, a hydrocarbon (15 g.), b. p. 230—232°/25 mm., crystallising from ethanol in needles, m. p. 95°. Cook and Hewett (*J.*, 1934, 365) gave m. p. 99° for this hydrocarbon.

Cyclodehydrogenation of 2-2′-Phenylethylnaphthalene.—A mixture of the foregoing hydrocarbon (10 g.), powdered aluminium chloride (10·5 g.), and carbon disulphide (100 c.c.) was refluxed for 4 hours. The brown reaction mixture was poured on cracked ice, the carbon disulphide was removed by steam-distillation, and the hydrocarbons were taken up in benzene. The benzene solution was dried (Na_2SO_4), the solvent removed, and the residue purified by vacuum-distillation. The solid distillate (3 g.) gave, after two recrystallisations from ethanol, shiny leaflets, m. p. 247°, which showed no m. p. depression on admixture with chrysene. Further proof of constitution was the chromic oxidation to chrysenequinone, m. p. 240°. The mother-liquors from the separation of chrysene were evaporated, and the residue crystallised from ethanol, thus giving a further crop of chrysene. Repetition of this process yielded finally a residue crystallising from ethanol in shiny leaflets, m. p. 160°, giving no m. p. depression on admixture with authentic 1 : 2-benzanthracene. In the mother-liquors from the separation of 1 : 2-benzanthracene, no trace of 3 : 4-benzophenanthrene could be detected.

Cyclodehydrogenation of 1 : 2-Di-2′-naphthylethane.—This hydrocarbon was easily prepared by Buu-Hoï and Hoán's procedure (*loc. cit.*). 10 G. of this compound were treated with aluminium chloride (10 g.) in carbon disulphide (100 c.c.) as in the foregoing instance. After the usual treatment and vacuum-distillation of the reaction-product, the portion (4 g.) of b. p. >350°/15 mm. was recrystallised twice from xylene, giving colourless sublimable leaflets, m. p. 365°, identical with an authentic sample of picene prepared according to Buu-Hoï and Hoán (*loc. cit.*). The xylene mother-liquors from the purification of picene were heated with maleic anhydride (Clar and Lombardi, *Ber.*, 1932, **65**, 1418); sublimation of the adduct thus obtained yielded 1 : 2-6 : 7-dibenzophenanthrene, crystallising from xylene in pale yellow sublimable leaflets, m. p. 293°. Clar (*Ber.*, 1929, **62**, 1578) gave for this hydrocarbon m. p. 293—294°.

2-Methyl-6-2′-phenylethylnaphthalene.—A mixture of 2-methyl-6-phenylacetylnaphthalene (5 g.) (prepared according to Buu-Hoï and Royer, *loc. cit.*, from very pure β-methylnaphthalene), 85% hydrazine hydrate (5 g.), potassium hydroxide (5 g.), and diethylene glycol (100 c.c.) was slowly heated to 200° with removal of water, and then refluxed for 4 hours. After routine treatment of the reaction-product, the *hydrocarbon* was obtained as a solid, b. p. 255—257°/35 mm., crystallising from ethanol in leaflets (3·5 g.), m. p. 94° (Found : C, 92·4; H, 7·3. $C_{19}H_{18}$ requires C, 92·7; H, 7·3%).

7-Methyl-1-2′-phenylethylnaphthalene.—This *hydrocarbon* (12 g.) was similarly obtained from 7-methyl-1-phenylacetylnaphthalene (Buu-Hoï and Royer, *loc. cit.*) (15 g.), 85% hydrazine hydrate (15 g.), potassium hydroxide (15 g.), and diethylene glycol (100 c.c.); it formed a pale yellow oil, b. p. 225—227°/19 mm. (Found : C, 92·5; H, 7·4. $C_{19}H_{18}$ requires C, 92·7; H, 7·3%). The picrate crystallised from ethanol in needles, m. p. 107°.

Cyclodehydrogenation of these isomeric compounds yielded intractable mixtures of hydrocarbons.

2 : 3-Dimethyl-6-phenylacetylnaphthalene.—To an ice-cooled mixture of 2 : 3-dimethylnaphthalene (40 g.), phenylacetyl chloride (40 g.), and nitrobenzene (250 c.c.), powdered aluminium chloride (45 g.) was added in small portions with stirring. The reaction product was kept overnight and then treated in the usual way. After purification by vacuum-distillation and recrystallisation from ethanol, the *ketone* was obtained as needles, m. p. 138° (Found : C, 87·5; H, 6·7. $C_{20}H_{18}O$ requires C, 87·6; H, 6·6%). The *oxime* formed, from ethanol, shiny prisms, m. p. 169° (Found : C, 83·2; H, 6·6. $C_{20}H_{19}ON$ requires C, 83·4; H, 6·6%).

2-(2 : 3-Dimethyl-6-naphthyl)-3-phenylcinchoninic Acid.—A mixture of the foregoing ketone (2 g.), isatin (1·2 g.), potassium hydroxide (1·3 g. dissolved in 2 c.c. of water), and ethanol (8 c.c.) was refluxed for 24 hours. After dilution with water and removal of the neutral impurities by ether-extraction, the reaction product yielded on acidification with acetic acid the *cinchoninic acid* (2·5 g.) which crystallised from ethanol in yellowish needles, m. p. 287—288° (shrinking above 270°) (Found : C, 83·2; H, 5·3. $C_{28}H_{21}O_2N$ requires C, 83·4; H, 5·2%). Heating of this acid above its m. p. and vacuum-distillation of the residue gave 2-(2 : 3-*dimethyl-6-naphthyl*)-3-*phenylquinoline* which crystallised from ethanol as shiny needles, m. p. 158° (Found : C, 90·0; H, 5·7. $C_{27}H_{21}N$ requires C, 90·2; H, 5·8%). The picrate of this base formed, from xylene, prisms, m. p. 248—249° (decomp.).

2 : 3-Dimethyl-6-2′-phenylethylnaphthalene.—2 : 3-Dimethyl-6-phenylacetylnaphthalene (23 g.), 85% hydrazine hydrate (23 g.), and potassium hydroxide (23 g.) in diethylene glycol (180 c.c.) gave the expected *hydrocarbon*, b. p. 240—242°/14 mm., crystallising from ethanol in needles, m. p. 120° (Found : C, 92·2; H, 7·9. $C_{20}H_{20}$ requires C, 92·3; H, 7·7%).

1-*Methyl*-4-2′-*phenylethylnaphthalene*.—The reduction of 1-methyl-4-phenylacetylnaphthalene (Cook and Galley, *loc. cit.*) gave a liquid *hydrocarbon*, b. p. 233—235°/14 mm. (Found: C, 92·8; H, 7·5. $C_{19}H_{18}$ requires C, 92·7; H, 7·3%), which formed a picrate, m. p. 114° (needles from ethanol).

3-2′-*Phenylethylpyrene*.—3-Phenylacetylpyrene was prepared according to Buu-Hoï and Royer (*Bull. Soc. chim.*, 1946, **13**, 659) and formed from ethanol–benzene needles, m. p. 115° (lit., m. p. 104°). Reduction of this ketone (8 g.) with 85% hydrazine hydrate (8 g.) and potassium hydroxide (8 g.) in diethylene glycol (100 c.c.) yielded a *hydrocarbon* crystallising from ethanol in prisms, m. p. 83° (Found: C, 94·3; H, 6·0. $C_{24}H_{18}$ requires C, 94·1; H, 5·9%).

4-2′-*Phenylethyldibenzyl*.—4-Phenylacetyldibenzyl (Buu-Hoï and Royer, *Rec. Trav. chim.*, 1946, **65**, 251) (38 g.), hydrazine hydrate (40 g.), and potassium hydroxide (40 g.) in diethylene glycol (250 c.c.) yielded the expected *hydrocarbon* (26 g.), b. p. 245—250°/13 mm., crystallising from ethanol in leaflets, m. p. 91° (Found: C, 92·2; H, 7·8. $C_{22}H_{22}$ requires C, 92·3; H, 7·7%). This compound yielded on cyclodehydrogenation a liquid product, possibly impure 3-2′-phenylethylphenanthrene.

4 : 4′-*Bisphenylacetyldibenzyl*.—This diketone was obtained in 50% yield in the Friedel–Crafts condensation of dibenzyl (50 g.) with phenylacetyl chloride (86 g.) in the presence of aluminium chloride (80 g.) in carbon disulphide (300 c.c.). It had b. p. 345—350°/13 mm. and crystallised from ethanol in needles, m. p. 179° (Found: C, 86·0; H, 6·5. $C_{30}H_{26}O_2$ requires C, 86·1; H, 6·2%).

4 : 4′-*Di*-(2-*phenylethyl*)*dibenzyl*.—This *hydrocarbon* crystallised from a mixture of ethanol–benzene in leaflets, m. p. 139° (Found: C, 90·0; H, 9·8. $C_{30}H_{30}$ requires C, 90·3; H, 9·7%).

2-2′-*Phenylethylthiophen*.—2-Phenylacetylthiophen (82 g.) was prepared from thiophen (42 g.), phenylacetyl chloride (80 g.), and aluminium chloride (68 g.) in carbon disulphide (250 c.c.) (30 minutes at room temperature). It gave on reduction with hydrazine hydrate (75 g.) and potassium hydroxide (70 g.) in diethylene glycol (400 c.c.) an 85% yield of 2-2′-*phenylethylthiophen*, b. p. 159—160°/13 mm., crystallising from methanol in leaflets, m. p. 109° (Found: C, 76·3; H, 6·5. $C_{12}H_{12}S$ requires C, 76·6; H, 6·4%). On treatment of this compound with aluminium chloride in carbon disulphide much hydrogen sulphide was evolved.

2 : 5-*Dimethyl*-3-2′-*phenylethylthiophen*.—2 : 5-Dimethyl-3-phenylacetylthiophen (Buu-Hoï and Hoán, *ibid.*, 1948, **67**, 309) gave on reduction a 70% yield of 2 : 5-*dimethyl*-3-2′-*phenylethylthiophen* as a pale yellow oil, b. p. 175—179°/13 mm. (Found: C, 77·5; H, 7·6. $C_{14}H_{16}S$ requires C, 77·8; H, 7·4%). Extensive evolution of hydrogen sulphide was also observed on treatment of this compound with aluminium chloride.

THE RADIUM INSTITUTE, UNIVERSITY OF PARIS. [*Received, December 27th*, 1950.]

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318. *The Mechanism of Decarboxylation. Part VI. Kinetics of the Acid-catalysed Decarboxylation of 2 : 4 : 6-Trihydroxybenzoic Acid.*

By B. R. BROWN, W. W. ELLIOTT, and D. LL. HAMMICK.

In continuation of the investigations described in Part V (Brown, Hammick, and Scholefield, *J.*, 1950, 778), the kinetics of the decarboxylation of 2 : 4 : 6-trihydroxybenzoic acid have been studied in aqueous solution. The effect of added mineral acid on the rate, *i.e.*,

$$\text{rate} = k[\text{R}\cdot\text{CO}_2\text{H}] + k_{\text{H}}[\text{H}_3\text{O}^+][\text{R}\cdot\text{CO}_2\text{H}]$$

is best interpreted on the basis of two simultaneous processes:

$$\text{(I)} \quad \text{R}\cdot\text{CO}_2^- + \text{H}_3\text{O}^+ \longrightarrow \text{R}\cdot\text{H} + \text{CO}_2 + \text{H}_2\text{O}$$

$$\text{or} \quad \text{R}\cdot\text{CO}_2\text{H} \longrightarrow \text{R}\cdot\text{H} + \text{CO}_2$$

$$\text{(II)} \quad \text{R}\cdot\text{CO}_2\text{H} + \text{H}_3\text{O}^+ \longrightarrow \text{R}\cdot\text{H} + \text{CO}_2 + \text{H}_3\text{O}^+$$

of which (I) can be regarded as either an $S_{\text{E}}1$ or an $S_{\text{E}}2$ mechanism, and (II) as an $S_{\text{E}}2$ mechanism. The activation energy of process (I) is found to be 21,500 cals.; that of process (II) is 15,200 cals.

THE process of decarboxylation is essentially a replacement reaction: $\boldsymbol{H} + \text{R}\cdot\text{CO}_2\text{H} \longrightarrow \boldsymbol{H}\cdot\text{R} + \text{CO}_2 + \text{H}$; such replacements in other molecular species (*e.g.*, replacement of halogen by OH in alkyl halides) have long been known to take place by the $S_{\text{E}}1$ and $S_{\text{E}}2$ processes of Hughes and Ingold (*J.*, 1935, 244), and in recent years evidence has accumulated that decarboxylation may occur by analogous $S_{\text{E}}1$ and $S_{\text{E}}2$ mechanisms (Schenkel and Schenkel-

Rudin, *Helv. Chim. Acta*, 1948, **31**, 514). An S_N1 mechanism would require the " loosening " of the R–C bond to be the rate-determining process, with the implication of a rate unaffected by acids and facilitated by the introduction of substituents into R that *diminish* electron density at the atom α to the carboxyl group (cf. Pedersen, *J. Physical Chem.*, 1934, **38**, 559; Verhoek, *J. Amer. Chem. Soc.*, 1939, **61**, 186). The rate of an S_E2 process will be determined by the attack of a proton (proton acid or protonated solvent) at the α-carbon atom and will show bimolecular kinetics involving " acid-catalysis " (Schubert, *J. Amer. Chem. Soc.*, 1949, **71**, 2639; Johnson and Heinz, *ibid.*, p. 2913). It will be facilitated by substituents in R that *increase* electron density at the α-carbon atom (Brown, Hammick, and Scholefield, *loc. cit.*).

2 : 4 : 6-Trihydroxybenzoic acid is decarboxylated readily in aqueous solution at 50° and thus appears suitable for investigation under conditions of varying pH. It should be possible not only to establish acid catalysis, if operative, but also to determine whether the undissociated acid or the anion is the decarboxylating species.

2 : 4 : 6-Trihydroxybenzoic acid may reasonably be expected to decarboxylate in aqueous solution by one or more of six mechanisms which fall kinetically into three groups :

(I) The unimolecular decomposition of the anion of the carboxylic acid, or the pseudo-unimolecular decomposition of the anion by interaction with a water molecule :

$$\begin{gathered} R{\cdot}CO_2^- \quad (+H_2O) \longrightarrow R^- + CO_2 \quad (+H_2O) \\ -dc/dt = k_1[R{\cdot}CO_2^-] = k_1\alpha c \end{gathered}$$

where c is the total concentration of the carboxylic acid whether dissociated or not, and α is the degree of dissociation of the acid.

(II) The bimolecular attack of a solvated proton on the α-carbon atom of the undissociated acid :

$$\begin{gathered} R{\cdot}CO_2H + H_3O^+ \longrightarrow R{\cdot}H + CO_2 + H_3O^+ \\ -dc/dt = k_2[H_3O^+][R{\cdot}CO_2H] = k_2\alpha(1-\alpha)c^2 \end{gathered}$$

(III) The bimolecular attack of a solvated proton on the α-carbon atom of the anion of the acid, or the unimolecular decomposition of the undissociated acid or the pseudo-unimolecular decomposition of the acid by interaction with a water molecule :

$$\begin{gathered} R{\cdot}CO_2^- + H_3O^+ \longrightarrow R{\cdot}H{\cdot} + CO_2 + H_2O \\ \text{or} \quad R{\cdot}CO_2H \quad (+H_2O) \longrightarrow R{\cdot}H{\cdot} + CO_2 + (H_2O) \\ \left.\begin{gathered} -dc/dt = k_3[H_3O^+][R{\cdot}CO_2^-] = k_3K(1-\alpha)c \\ \text{or} \quad -dc/dt \quad k_4[R{\cdot}CO_2H] \qquad = k_4(1-\alpha)c \end{gathered}\right\} = \text{constant} \times (1-\alpha)c \end{gathered}$$

where K is the dissociation constant of the acid.

These three mechanisms should be distinguishable by the effect of added mineral acid. Thus, according to mechanism (I) the rate of reaction should be retarded by added hydrochloric acid since α will decrease; according to mechanism (II) the rate will be markedly increased by the addition of acid since both $[H_3O^+]$ and $[R{\cdot}CO_2H]$ will be increased; according to mechanism (III), however, the rate will be only slightly increased since the term $(1-\alpha)$ increases only slightly with added acid.

Experimental.

The decarboxylation was followed by removing samples of the acid solution with a pipette. Each sample was treated with excess of cold standard potassium hydroxide solution, which effectively stops the reaction, and the excess of alkali was back-titrated with standard hydrochloric acid. The indicator used was methyl-red and the titration was carried to a definite pink tint (pH *ca.* 4). A small correction was then applied (0·05 ml.) to allow for the change from the true end-point to pH 4. This correction was determined by means of a Cambridge pH meter. By this means it was not found necessary to remove dissolved carbon dioxide, which buffers the solution at pH *ca.* 6, since sharp end-points were obtained.

Temperature control to within 0·05° was ensured by means of a water thermostat. All volumetric instruments were standardised by weight at the temperature at which they were required to function.

In Table I the rate constants are given at various temperatures and at various concentrations of hydrochloric acid. In col. 3 the rate constants are those calculated assuming that mechanism (I) controls the rate, col. 4 those assuming mechanism (II), and col. 5 those assuming that mechanism (III) controls the rate. All reactions were carried out at constant ionic strength, 1·08N. with respect to HCl and KCl, in order to standardise salt effects.

TABLE I.

Temp., ° K.	Concn. of added HCl, N.	Coeff. × 10^3, sec.$^{-1}$ (I)	Coeff. × 10^3, l. mol.$^{-1}$ sec.$^{-1}$ (II)	Coeff. × 10^3, sec.$^{-1}$ (III)	Temp., ° K.	Concn. of added HCl, N.	Coeff. × 10^3, sec.$^{-1}$ (I)	Coeff. × 10^3, l. mol.$^{-1}$ sec.$^{-1}$ (II)	Coeff. × 10^3, sec.$^{-1}$ (III)
323·0	nil	—	135	1·09	318·2	nil	—	68·3	0·613
—	0·0458	2·94	23·9	1·19	—	0·0346	1·45	19·4	0·750
—	0·0476	3·11	23·5	1·21	—	0·0417	1·79	17·6	0·794
—	0·0541	3·87	23·5	1·30	—	0·0484	2·09	15·7	0·780
—	0·0714	4·95	18·5	1·34	—	0·0550	2·28	14·3	0·822
—	0·0853	6·18	15·4	1·35	—	0·0613	2·54	13·1	0·791
—	0·1145	8·89	12·9	1·53	—	0·0680	2·83	11·6	0·808
—	0·1474	11·5	10·3	1·57	—	0·0742	3·16	10·9	0·832
—	0·1783	16·4	10·0	1·76	—	0·0804	3·43	10·0	0·826
312·95	nil	— *	42·2	0·356	—	0·0866	4·13	10·5	0·924
—	0·0346	0·80	11·1	0·421	—	0·1000	4·73	9·5	0·948
—	0·0412	0·91	9·9	0·436	—	0·1162	5·62	8·2	0·960
—	0·0553	1·26	7·7	0·441	—	0·1218	6·02	7·5	0·948
—	0·0671	1·86	7·9	0·497	—	0·1278	5·65	7·7	0·997
—	0·0795	2·26	6·8	0·550					
—	0·0973	2·80	5·6	0·552					
—	0·1091	2·92	5·0	0·550					
—	0·1260	3·90	4·8	0·608					

* If mechanism (I) is assumed to control the rate, a linear logarithmic plot is not obtained in the absence of added mineral acid.

TABLE II.

Amine.	10^4a (mol./l.).	10^3k_4 (sec.$^{-1}$).	Amine.	10^4a (mol./l.).	10^3k_4 (sec.$^{-1}$).
p-$C_6H_4Me{\cdot}NH_2$ ...	nil	2·90	Ph·NHMe	7·8	3·14
	1·5	3·05		12·0	3·35
	10·4	3·34		19·5	3·70
	17·0	3·62			
			Ph·NMe_2	7·0	3·10
				11·2	3·40
				17·0	3·64

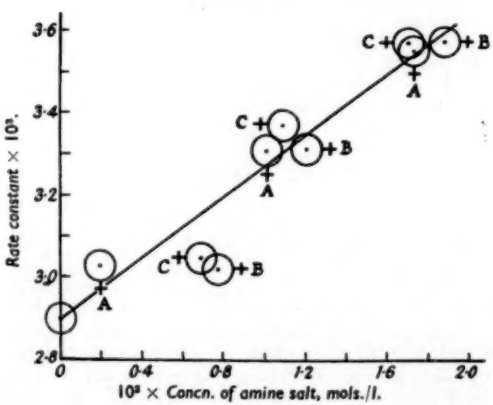
Temp., 333·2° K. c, ~ 0·004M.

The rate constants obtained in the presence of various aromatic amines are given in Table II and Fig. 1. They have been calculated by assuming that mechanism (III) alone controls the rate :

$$-dc/dt = k_4[R{\cdot}CO_2H] = k_4(1 - a)(c - a)$$

where a is the concentration of added amine and c is the total concentration of carboxylic acid, *i.e.*, free acid plus amine salt of the acid. The values of c were determined experimentally by titration against standard barium hydroxide, bromocresol-purple being used as indicator (pK 6·3) after the dissolved carbon dioxide had been removed in a stream of nitrogen.

FIG. 1.



⊙ + A p-*Toluidine.* ⊙+B. N-*Methylaniline.* C+⊙. NN-*Dimethylaniline.*

Discussion of Results.

From Table I it will be seen that cols. 3 and 4 do not provide a constant value for the rate constant and hence mechanisms (I) or (II) cannot be held to control the rate of reaction. The rate constants in col. 5 increase, at all three temperatures, by about 50% over the range 0—0·12N-HCl. This increase is too large and too regular to be due to experimental error and therefore mechanism (III) cannot be considered to be the rate-controlling step. Therefore, since no single assumption as to the mechanism provides a true rate constant, the actual decomposition must be composite. One of the components of the reaction must be mechanism (II), the bimolecular attack of a proton on the undissociated acid, since mechanism (III) cannot account for the magnitude of the catalytic effect of added hydrogen ions and mechanism (I) would be inhibited by added hydrogen ions. Either or both of mechanisms I and III may, however, contribute to the total effect.

In order to estimate the magnitude of the contribution of mechanism (I), the reaction was carried out at pH *ca.* 7, where only mechanism (I) can operate appreciably. It is known that the anion is decarboxylated according to the equilibrium equation:

$$R{\cdot}CO_2^- + H_3O \rightleftharpoons RH + HCO_3^-$$

the equilibrium constant at 50° being 0·11 (Hallstrom, *Ber.*, 1905, **38**, 2288). Employing this value of the equilibrium constant and also by the method of initial rates we find that this reaction, which is extremely slow at 50°, cannot contribute more than 0·25% to the total reaction in acidic solution. This contribution to the composite decomposition is within the experimental error and has been ignored.

We now proceed with the assumption that the second component must be mechanism (III). The total reaction may be thus expressed by the differential equation

$$-dc/dt = k_2[H_3O^+][R{\cdot}CO_2H] + k_4[R{\cdot}CO_2H]$$

where k_4 may equal k_2K (see p. 1385).

The individual rate constants may be determined by adding such an excess of hydrogen chloride that the reaction is unimolecular or pseudo-unimolecular and the term $(1 - \alpha)$ is virtually constant in any single run. Then by integration

$$-2{\cdot}303 \log c = [k_2[H_3O^+](1 - \alpha) + k_4(1 - \alpha)]t + i$$

and hence by a plot of $-\log c$ against time

$$\text{slope} \times 2{\cdot}303 = k_2[H_3O^+](1 - \alpha) + k_4(1 - \alpha)$$

From this it follows that a plot of slope $\times$ $2{\cdot}303/(1 - \alpha)$ against $[H_3O^+]$ has a slope of k_2 and an intercept of k_4. In Fig. 2 this procedure has been adopted. The rate constants thus

Table III.

Temp. ° K.	312·95	318·2	323·0
10^3k_2 (l. mol.$^{-1}$ sec.$^{-1}$)	1·84	2·45	3·90
10^3k_2K or 10^3k_4 (sec.$^{-1}$)	0·359	0·67	1·04

obtained are given in Table III, and the Arrhenius energies of activation are obtained from these rate constants by Fig. 3 and tabulated in Table IV.

Table IV.

	Mechanism.	E_a. cals.	PZ factor.
(II)	Acid + proton	15,200	$6{\cdot}7 \times 10^7$ (l./mol.$^{-1}$ sec.$^{-1}$)
(III)	Anion + proton	21,500	$2{\cdot}0 \times 10^{13}$ (l./mol.$^{-1}$ sec.$^{-1}$)
	or		
	Acid unimolecular		$4{\cdot}0 \times 10^{11}$ (sec.$^{-1}$)

The energy of activation obtained by Brown, Hammick, and Scholefield (*loc. cit.*) for 2 : 4 : 6-trihydroxybenzoic acid in resorcinol is 13,600 cals., and the *PZ* factor is 10^8. These values are thought to refer to the reaction between the undissociated acid and the acidic solvent and are thus to some extent comparable with the reaction between the undissociated acid and the solvated proton given above.

No great precision can be attributed to our energies of activation owing to (i) the complicated nature of the reaction; (ii) the variation in dissociation constant K with temperature being ignored and, though probably small, is not likely to be negligible; (iii) and the small temperature range allowed by considerations of solubility and speed of reaction.

FIG. 2.

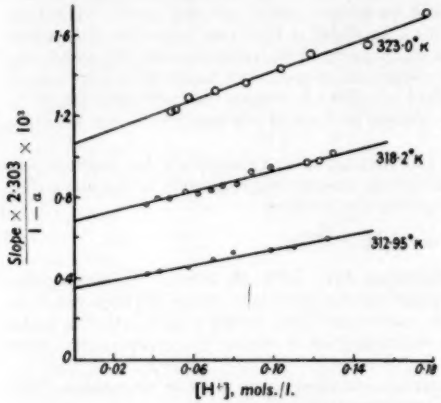
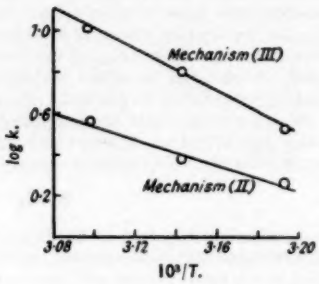
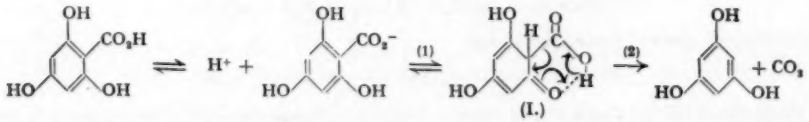


FIG. 3.



These results do not differentiate between the unimolecular decomposition of the undissociated acid and the bimolecular attack of a proton on the α-carbon atom of the anion. This is due to the fundamental similarity of the two reactions from a kinetic standpoint. If the acid decomposes unimolecularly it is likely that the tautomeric keto-form will be the decarboxylating species. This acid forms a trioxime and since the keto-form would be a β-keto-acid, it might be expected to be readily decarboxylated. The following equilibria may therefore be possible:



Thus the difference between a unimolecular decomposition of the acid and a bimolecular reaction between a proton and an anion may depend on whether (1) or (2) is the rate-determining step. Both mechanisms would probably pass through an intermediate of structure (I). If this intermediate is very unstable then (1) will be rate determining, and the reaction will be of the S_E2 type. On the other hand, if (I) is fairly stable, (2) will be the rate-determining step, and the mechanism will be of the S_E1 type. For the S_E2 mechanism (I) must be regarded as an activated transition state; for the S_E1 mechanism (I) is regarded as the stable keto-form of the hydroxy-acid. Hence the two mechanisms probably cannot be differentiated, since they give rise to the same kinetic equation and both pass through the same intermediate. They cannot be differentiated by a primary salt effect since the activity of the intermediate complex, an uncharged species, is the same as that of the free acid. A secondary salt effect has been demonstrated but it may be shown that this is of no diagnostic significance.

However, a comparison of the effect of primary, secondary, and tertiary amines may be of some value. Pedersen (*loc. cit.*) reports that the decarboxylation of acetoacetic acid is markedly catalysed by primary amines, slightly by secondary amines, and hardly at all by tertiary amines. This was held to be due to the interaction of the keto-group with the primary amine. The decarboxylation of 2 : 4 : 6-trihydroxybenzoic is, however, catalysed equally, within the limits of experimental error, by primary, secondary, and tertiary amines (see Fig. 1). This amine catalysis may be attributed to general acid catalysis by the ammonium ions formed in acid solution, and the small magnitude of the effect may be due to the small catalytic power of the weak acid $\rangle\overset{+}{N}—H$ as compared to that of H_3O^+. In the absence of specific catalysis by primary

amines, we therefore infer that mechanism (III) is probably the attack of a proton on the α-carbon atom of the anion, and that the anion may be decarboxylated by a water molecule (mechanism I), an ammonium ion, and also by an oxonium ion (mechanism III). The magnitude of the catalytic effects are $H_3O^+ > \overset{\diagdown}{\underset{\diagup}{\overset{+}{N}}}—H > H_2O$. The experiments on the effect of added amines were carried out at high dilutions where mechanism (II) contributes less than 5% to the total reaction, since the acid is almost completely dissociated.

It is therefore concluded that 2 : 4 : 6-trihydroxybenzoic acid is decarboxylated in acidic solution by at least three mechanisms :

(I)	anion + water molecule	very slow
(II)	acid + oxonium ion	fast
(III)	anion + oxonium ion	fast

In the absence of added hydrogen chloride, (III) is the main contributor to the total reaction, but in the presence of excess of hydrogen chloride (II) and (III) are equally important.

In all the above calculations the value of the acid dissociation constant used is 2×10^{-2}. Ostwald (*Z. physikal. Chem.*, 1889, **3**, 253) determined K at 25° to be $2{\cdot}1 \times 10^{-2}$. We, however, have worked at temperatures of 40—50° and at high salt strength (1·08N.). On using a Cambridge pH meter at 20° and salt strength 1·08N., a value of $2{\cdot}0 \pm 0{\cdot}3 \times 10^{-2}$ was obtained, but since this is a difficult region of acidic strength to determine accurately, this value must be regarded as approximate only. It is fortunate, however, that our deductions are largely independent of the value of the dissociation constant since α varies as $\sqrt{K}$; $(1 - \alpha)$ in the presence of excess of hydrogen chloride is even less dependent on K. Indeed, even if K were as large as 5×10^{-2}, the above deductions as to the mechanism would hold though the actual values of the rate constants would be different. Only if K were as large as 7×10^{-2} would our deductions be invalid and a single mechanism, *i.e.*, (III) would hold. The effect of temperature on K should be, by analogy with other strong acids, both organic and inorganic, to decrease K with increasing temperature; such an effect would operate to the advantage of our conclusions.

THE DYSON PERRINS LABORATORY, UNIVERSITY OF OXFORD. [*Received, December 21st*, 1950.]

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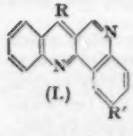
319. *Attempts to find New Antimalarials. Part XXX. The Synthesis of Derivatives of Quinolino(4′ : 3′-2 : 3)quinoline.*

By WILLIAM O. KERMACK and (MRS.) NORA E. STOREY.

4-Anilinoquinoline-3-carboxylic acid and its derivatives are cyclized in concentrated sulphuric acid to the corresponding 4-hydroxyquinolino-(4′ : 3′-2 : 3)quinolines (I; R = OH), and with phosphorus oxychloride and pentachloride yield the analogous 4-chloroquinolino(4′ : 3′-2 : 3)quinolines (I; R = Cl). The halogen atom in the 4-position in these bases is stable to alkali but readily hydrolysed in the presence of acid and is replaced by the dialkylaminoalkylamino-group under conditions similar to those used for the isomeric 5-chloropyridoacridines which the quinolinoquinolines closely resemble.

QUINOLINO(4′ : 3′-2 : 3)QUINOLINE (I; R = R′ = H) was first prepared by Clemo and Perkin (*J.*, 1924, **125**, 1608) who condensed 4-keto-1 : 2 : 3 : 4-tetrahydroquinoline with isatin and isolated the decarboxylated product, 1′ : 2′-dihydroquinolino(4′ : 3′-2 : 3)quinoline. This compound on distillation over lead oxide lost two atoms of hydrogen. Mann (*Nature*, 1949, **164**, 785; *J.*, 1949, 2816) has recently carried out similar reactions using 4-keto-1-phenyl-1 : 2 : 3 : 4-tetrahydroquinoline instead of 4-keto-1 : 2 : 3 : 4-tetrahydroquinoline and so obtained 1′ : 2′-dihydro-1′-phenylquinolino(4′ : 3′-2 : 3)quinoline, the salts of which are highly coloured, apparently owing to electromeric effects in the anion.



(I.)

In view of the considerable antimalarial activity of certain derivatives of pyridino(4′ : 3′-2 : 3)acridine carrying a basic side-chain in the 5-position it was considered desirable to synthesise analogous derivatives of quinolino(4′ : 3′-2 : 3)quinoline. An attempt was first made to prepare 4-chloroquinoline-3-carboxylic acid as it was thought that

this, by condensation with aniline, would readily yield 4-anilinoquinoline-3-carboxylic acid which could then be cyclized with the formation of 4-chloroquinolino(4′ : 3′-2 : 3)quinoline (I; R = Cl, R′ = H), a compound in which the chlorine atom, as in the corresponding 5-chloroacridine, should be readily replaceable by appropriate basic side chains.

Ethyl 4-hydroxyquinoline-3-carboxylate was easily converted into ethyl 4-chloroquinoline-3-carboxylate but hydrolysis of the ester group invariably resulted in the removal of chlorine with the formation of 4-hydroxyquinoline-3-carboxylic acid and so far we have been unable to prepare 4-chloroquinoline-3-carboxylic acid from the 4-hydroxy-acid. Ethyl 4-anilinoquinoline-3-carboxylate was however obtained by condensing ethyl 4-chloroquinoline-3-carboxylate with aniline followed by hydrolysis of the ester. The acid, which could not be easily recrystallised because of its tendency to form gels, yielded 4-anilinoquinoline on decarboxylation, and its identity was thus confirmed. On treatment with sulphuric acid at 100° 4-anilinoquinoline-3-carboxylic acid cyclized to give 4-hydroxyquinolino(4′ : 3′-2 : 3)quinoline, whilst with phosphorus oxychloride it yielded 4-chloroquinolino(4′ : 3′-2 : 3)quinoline. The chlorine atom in this compound is readily split off by acids with formation of the 4-hydroxy-derivative, but the compound is stable to alkali and can be recrystallised unchanged from aqueous alcohol.

The 4-chloroquinolinoquinoline and its derivatives closely resemble 5-chloroacridine; in particular they are stable to alkali but are converted into the 4-hydroxyquinolinoquinolines in the presence of acid. The 4-chloroquinolinoquinolines are comparatively more stable to a hot solution of aqueous alcohol, but like 5-chloroacridines tend to give poor analytical data, indicating the presence of traces of the corresponding 4-hydroxy-compounds.

Attempts to prepare 4-chloro-6-methoxyquinoline-3-carboxylic acid from the 4-hydroxy-6-methoxy-acid or by hydrolysis from ethyl 4-chloro-6-methoxyquinoline-3-carboxylate failed, the chlorine atom being very readily hydrolysed as in the case of the corresponding compound without the methoxy-group. On the other hand, crude 4 : 6-dichloroquinoline-3-carboxylic acid was obtained from 6-chloro-4-hydroxyquinoline-3-carboxylic acid by treatment with phosphorus oxychloride and pentachloride. The presence of the chlorine atom in the 6-position evidently increases the stability of that in position 4; similar effects in the quinoline series have been observed by Drake *et al.* (*J. Amer. Chem. Soc.*, 1946, **68**, 1208). 4-Anilino-6-methoxyquinoline-3-carboxylic acid was obtained by condensing ethyl 4-chloro-6-methoxyquinoline-3-carboxylate with aniline and hydrolysing the product. 4 : 6-Dichloroquinoline-3-carboxylic acid condensed readily with aniline to yield 4-anilino-6-chloroquinoline-3-carboxylic acid. These two derivatives of 4-anilinoquinoline-3-carboxylic acid, when treated with warm sulphuric acid, yielded respectively 4-hydroxy-6′-methoxy- and 6′-chloro-4-hydroxy-quinolino(4′ : 3′-2 : 3)quinoline (I; R = OH, R′ = OMe and R = OH, R′ = Cl), and on treatment with phosphorus oxychloride they gave respectively 4-chloro-6′-methoxy- and 4 : 6′-dichloro-quinolinoquinoline.

These two 4-chloroquinolinoquinolines and also 4-chloroquinolino(4′ : 3′-2 : 3)quinoline itself could also be prepared from the corresponding 4-hydroxyquinolinoquinolines by refluxing them with phosphorus oxychloride containing phosphorus pentachloride. The yield in this reaction was usually poor but it was increased if a small quantity of hexadecyltrimethylammonium bromide ("Cetavlon") was added to the mixture before it was refluxed. For example, in the conversion of 4-hydroxy-6′-methoxyquinolino(4′ : 3′-2 : 3)quinoline to the 4-chloro-6′-methoxy-compound, the yield improved from 31% to 47% when "Cetavlon" was added. The mechanism whereby "Cetavlon" effects this improvement is not known, but reference may be made to its advantageous action in the preparation of 3-chloro-2-naphthoic acid from 3-hydroxy-2-naphthoic acid (Cairns and Kermack, *J.*, 1950, 1322) and to the advantageous action of the addition of surface-active agents in the preparation of anilides from 3-hydroxy-2-naphthoic acid in the presence of phosphorus pentachloride (see U.S.P. 2,394,279/1946).

4-Chloroquinolinoquinoline and its analogues react with alkylaminoalkylamines in the presence of phenol. In this way 4-(2-diethylaminoethylamino)quinolino(4′ : 3′-2 : 3)quinoline and 4-(4-diethylamino-1-methylbutylamino)-6′-methoxyquinolino(4′ : 3′-2 : 3)quinoline have been prepared.

These quinolinoquinoline derivatives carrying a basic side chain form yellow solids which readily dissolve in dilute acid to give yellow solutions with green fluorescence, and in general resemble the isomeric pyridoacridines. When analysed these bases gave satisfactory carbon and hydrogen values but micro-Dumas determinations of nitrogen gave results 1—3% below the theoretical values. When however the temperature of the combustion tube was raised to 900°, nitrogen figures within 0·5% of the theoretical result were obtained. This experience is similar to that reported by Braucone and Fulmon (*Analyt. Chem.*, 1949, **21**, 1147).

Experimental.

(M. p.s are uncorrected.)

Ethyl 4-*Chloroquinoline*-3-*carboxylate*.—Ethyl 4-hydroxyquinoline-3-carboxylate (5·4 g.) was refluxed with phosphorus pentachloride (5·2 g.) and phosphorus oxychloride (10 c.c.) for 2 hours. The cold solution was poured on crushed ice, decolorized (charcoal), and basified with dilute sodium hydroxide. *Ethyl* 4-*chloroquinoline*-3-*carboxylate* crystallised from light petroleum (b. p. 40—60°) in large white prisms, m. p. 37° (Found: C, 61·1; H, 3·9; N, 5·6. $C_{13}H_{10}O_2NCl$ requires C, 61·15; H, 4·2; N, 5·9%).

Ethyl 4-*Anilinoquinoline*-3-*carboxylate*.—Ethyl 4-chloroquinoline-3-carboxylate (2·3 g.) and aniline (0·9 g.) reacted almost immediately with evolution of heat when mixed thoroughly at room temperature, the product setting to a hard golden gum. Dissolution of this in water and basification with ammonia solution yielded *ethyl* 4-*anilinoquinoline*-3-*carboxylate*, which crystallised from ethanol in short yellow prisms, m. p. 99—100° (Found: C, 74·0; H, 5·5; N, 9·6. $C_{18}H_{16}O_2N_2$ requires C, 73·7; H, 5·5; N, 9·9%).

4-*Anilinoquinoline*-3-*carboxylic Acid*.—4-Anilinoquinoline-3-carboxylate was hydrolysed for 1 hour with 5% ethanolic sodium hydroxide; subsequent neutralization with dilute acetic acid yielded 4-*anilinoquinoline*-3-*carboxylic acid* as a soapy gelatinous precipitate, m. p. 260—265° (Found: N, 11·0. $C_{16}H_{12}O_2N_2$ requires N, 10·6%). The product on being heated at its melting point was decarboxylated and yielded 4-anilinoquinoline, m. p. 196—198° (Ephraim, *Ber.*, 1893, **26**, 2229, gives m. p. 198°).

4-*Hydroxyquinolino*(4′ : 3′-2 : 3)*quinoline*.—4-Anilinoquinoline-3-carboxylic acid (0·5 g.) was heated at 95° with concentrated sulphuric acid (5 c.c.) for 30 minutes. A marked fluorescence developed which intensified as the heating continued. The cooled solution was poured on ice and basified with ammonia solution, yielding 4-*hydroxyquinolino*(4′ : 3′-2 : 3)*quinoline*. Recrystallised from ethanol, this formed long slender white fibres, which turned yellow on being dried. When these were moistened with water, the yellow colour disappeared and the colourless compound was regenerated. This had m. p. >360° (marked decomp.) (Found: C, 73·7; H, 4·2; N, 10·0. $C_{18}H_{10}ON_2,0·75H_2O$ requires C, 74·0; H, 4·4; N, 10·7%).

4-*Chloroquinolino*(4′ : 3′-2 : 3)*quinoline*.—4-Anilinoquinoline-3-carboxylic acid (1 g.) was refluxed with phosphorus oxychloride (5 c.c.) for 2 hours. The excess of phosphorus oxychloride was distilled off under reduced pressure at 80°, and the residual yellow powder, dried as far as possible at the pump, was triturated with cold 20% sodium hydroxide solution. The brownish-red solid was filtered off, washed with water, and dried in a vacuum desiccator (KOH). When the product was digested with hot benzene in the presence of a pellet of potassium hydroxide, some 4-hydroxyquinolino(4′ : 3′-2 : 3)quinoline remained undissolved; the 4-*chloroquinoline*(4′ : 3′-2 : 3)*quinoline*, m. p. 210—215°, crystallised from the benzene solution on cooling. It recrystallised from dry toluene in pale yellow cubes, m. p. 210° (Found: C, 73·2; H, 3·2; N, 10·2. $C_{18}H_9N_2Cl$ requires C, 72·6; H, 3·4; N, 10·6%). This compound was also prepared by refluxing 4-hydroxyquinolino(4′ : 3′-2 : 3)quinoline with phosphorus oxychloride and pentachloride for 6 hours.

Ethyl 4-*Chloro*-6-*methoxyquinoline*-3-*carboxylate*.—Ethyl 4-hydroxy-6-methoxyquinoline-3-carboxylate (15·5 g.) when refluxed with phosphorus oxychloride (20 c.c.) and pentachloride (13 g.) yielded *ethyl* 4-*chloro*-6-*methoxyquinoline*-3-*carboxylate*; this, when crystallised from light petroleum (b. p. 80—100°), had m. p. 84—86° (Found: N, 5·4. $C_{13}H_{12}O_3NCl$ requires N, 5·3%).

Ethyl 4-*Anilino*-6-*methoxyquinoline*-3-*carboxylate*.—Ethyl 4-chloro-6-methoxyquinoline-3-carboxylate (4·3 g.) and aniline (1·6 g.) were allowed to react at room temperature. *Ethyl* 4-*anilino*-6-*methoxyquinoline*-3-*carboxylate* was obtained as a white powder by the addition of ammonia solution to the hot aqueous solution of the resulting hydrochloride; recrystallised from ethanol it formed prisms, m. p. 101° (Found: N, 8·5. $C_{19}H_{18}O_2N_2$ requires N, 8·7%).

4-*Anilino*-6-*methoxyquinoline*-3-*carboxylic Acid*.—Ethyl 4-anilino-6-methoxyquinoline-3-carboxylate (20 g.) was hydrolysed by refluxing it with 5% ethanolic sodium hydroxide (100 c.c.) for 2 hours. When the product was precipitated by dilute acid it was obtained as a gelatinous compound which could not be crystallised from any of the ordinary solvents. 4-*Anilino*-6-*methoxyquinoline*-3-*carboxylic acid* was purified by dissolving it in dilute sodium carbonate solution and reprecipitating the acid with dilute acetic acid. It had m. p. 264° (frothing) (Found: C, 65·1; H, 4·9; N, 9·2. $C_{17}H_{14}O_3N_2,H_2O$ requires C, 65·3; H, 5·1; N, 9·0%).

4-*Hydroxy*-6′-*methoxyquinolino*(4′ : 3′-2 : 3)*quinoline*.—4-Anilino-6-methoxyquinoline-3-carboxylic acid (0·5 g.) when heated in concentrated sulphuric acid (5 c.c.) for 30 minutes yielded 4-*hydroxy*-6′-*methoxyquinolino*(4′ : 3′-2 : 3)*quinoline*, which was isolated after dilution and precipitation with ammonia solution; it had m. p. 350° (marked decomp.) (Found: C, 74·0; H, 4·5; N, 9·7. $C_{17}H_{12}O_2N_2$ requires C, 73·9; H, 4·7; N, 9·4%).

4-*Chloro*-6′-*methoxyquinolino*(4′ : 3′-2 : 3)*quinoline*.—4-Anilino-6-methoxyquinoline-3-carboxylic acid (1 g.) was heated in phosphorus oxychloride (30 c.c.) for 4 hours, and the product isolated as described for 4-chloroquinolino(4′ : 3′-2 : 3)quinoline. 4-*Chloro*-6′-*methoxyquinolino*(4′ : 3′-2 : 3)*quinoline* crystallised from toluene in long shining yellow needles, m. p. 177—178° (Found: C, 66·9, 67·1; H, 3·7, 4·3; N, 8·6, 8·5. $C_{17}H_{11}ON_2Cl,0·5H_2O$ requires C, 67·2; H, 3·95; N, 9·2%). This compound was also prepared by the action of phosphorus oxychloride and phosphorus pentachloride on 4-hydroxy-6′-methoxyquinolino(4′ : 3′-2 : 3)quinoline. The addition of "Cetavlon" (0·1 g.) to the reaction mixture increased the yield from 34% to 47%.

4-*Anilino*-6-*chloroquinoline*-3-*carboxylic Acid*.—6-Chloro-4-hydroxyquinoline-3-carboxylic acid (5 g.) was refluxed with phosphorus pentachloride (5·2 g.) and phosphorus oxychloride (15 c.c.) for 5 hours. When cold, the solution was poured on ice, and the resultant precipitate collected and dried in a vacuum over potassium hydroxide; it had m. p. 280—282° [the mixed m. p. with 6-chloro-4-hydroxyquinoline-3-

carboxylic acid (m. p. 278—279°) was 274°]. The crude dichloro-acid was used for the next stage in the synthesis as attempts to purify it resulted in loss of chlorine.

Crude 4 : 6-dichloroquinoline-3-carboxylic acid (8 g.) and aniline (2·3 g.) were mixed and warmed in a water-bath whereupon a reaction took place and the product set to a gum. *6-Chloro-4-anilinoquinoline-3-carboxylic acid* could not be obtained crystalline; it softened at 230° and had m. p. 260—262° (Found : N, 9·1. $C_{16}H_{11}O_2N_2Cl$ requires N, 9·4%).

6′-Chloro-4-hydroxyquinolino(4′ : 3′-2 : 3)*quinoline.*—4-Anilino-6-chloroquinoline-3-carboxylic acid was cyclized in concentrated sulphuric acid at 100°, giving *6′-chloro-4-hydroxyquinolino*(4′ : 3′-2 : 3)*quinoline*. The product, white needles (from ethanol), melted at >360° (Found : N, 10·0. $C_{16}H_9ON_2Cl$ requires N, 10·0%).

4 : 6′-Dichloroquinolino(4′ : 3′-2 : 3)*quinoline.*—4-Anilino-6-chloroquinoline-3-carboxylic acid (5 g.) was refluxed for 7 hours with phosphorus pentachloride (3 g.) and phosphorus oxychloride (20 c.c.) containing " Cetavlon " (0·1 g.). The product was isolated as described for the 4-chloro-compound. *4 : 6′-Dichloroquinolino*(4′ : 3′-2 : 3)*quinoline* crystallised from toluene as long white glistening fibres, m. p. 238° (Found : C, 63·4; H, 2·5; N, 9·4. $C_{16}H_8N_2Cl_2,0{\cdot}25H_2O$ requires C, 63·3; H, 2·8; N, 9·2%). This compound was also prepared by the action of phosphorus oxychloride on 6′-chloro-4-hydroxyquinolino(4′ : 3′-2 : 3)quinoline.

4-(2-Diethylaminoethylamino)quinolino(4′ : 3′-2 : 3)*quinoline.*—Freshly distilled phenol (5 g.) was heated in a vacuum on a steam-bath, and after 2 hours 2-diethylaminoethylamine (0·46 g.) was added, and the contents of the flask kept at 100° under vacuum for a further 2 hours. Dry 4-chloroquinolino-(4′ : 3′-2 : 3)quinoline (0·5 g.) was introduced, and the mixture heated at 100° under reflux. After 4 hours the cooled solution was poured into 2N-sodium hydroxide solution (30 c.c.), and the oily suspension extracted immediately with ether. The base was further purified by extraction of the ethereal solution with N-acetic acid, precipitation with ammonia solution, and re-extraction with ether. The ethereal solution was dried (K_2CO_3) and the ether removed. *4-(2-Diethylaminoethylamino)quinolino*(4′ : 3′-2 : 3)*quinoline* was crystallised from light petroleum (b. p. 80—100°); it formed rod-shaped crystals, m. p. 80—82° (Found : C, 76·65; H, 6·6; N, 15·9. $C_{22}H_{34}N_4$ requires C, 76·7; H, 6·9; N, 16·3%).

4-(4-Diethylamino-1-methylbutylamino)-6′-methoxyquinolino(4′ : 3′-2 : 3)*quinoline.*—A mixture of phenol (3 g.) and 2-amino-5-diethylaminopentane (1·5 g.) was dried under vacuum at 100° for 1 hour. Dry 4-chloro-6′-methoxyquinolino(4′ : 3′-2 : 3)quinoline (1 g.) was added, the dark-red solution heated under reflux at 100° for 4 hours, and the product worked up as described in the previous experiment. *4-(4-Diethylamino-1-methylbutylamino)-6′-methoxyquinolino*(4′ : 3′-2 : 3)*quinoline* crystallised from light petroleum (b. p. 60—80°) in long yellow prisms, m. p. 98—100° (Found : C, 75·2; H, 7·4; N, 13·4. $C_{24}H_{32}ON_4$ requires C, 75·0; H, 7·7; N, 13·5%).

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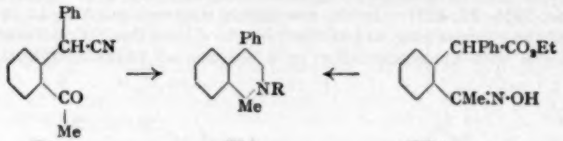
320. *The Synthesis of Piperidine Derivatives. Part V. Decahydroisoquinolines.*

By G. M. BADGER, J. W. COOK, and G. M. S. DONALD.

Reductive cyclisation of α-2-acetyl*cyclo*hexylbenzyl cyanide (I) in alcoholic solution by means of hydrogen and a copper chromite catalyst gave two stereoisomeric 2-alkyldecahydro-1-methyl-4-phenyl*iso*quinolines (II), the *N*-alkyl group being provided by the alcohol used as solvent. Hydrogenation of the oxime-ester (III) in methanol also gave some (II; R = Me) together with two stereoisomeric intermediates, decahydro-3-keto-1-methyl-4-phenyl*iso*quinoline (V). The Michael condensation product (XII) of malonamide and 1-phenylacetyl*cyclo*hex-1-ene was converted, through two intermediates, into 1-benzyldecahydro*iso*quinoline (X), which is a structural simplification of Grewe's *N*-methylmorphinan.

IN continuation of previous work on the synthesis of piperidine derivatives of possible pharmacological interest as analgesics and spasmolytics, we have now investigated the formation of certain aryldecahydro*iso*quinolines. The methods of reductive cyclisation developed in earlier papers of this series (Barr and Cook, *J.*, 1945, 438; Badger, Cook, and Walker, *J.*, 1948, 2011; 1949, 1141) have again been employed. The synthesis of decahydro-2-methyl-10-phenyl*iso*quinoline has been recorded recently by Boekelheide and Schilling (*J. Amer. Chem. Soc.*, 1950, **72**, 712).

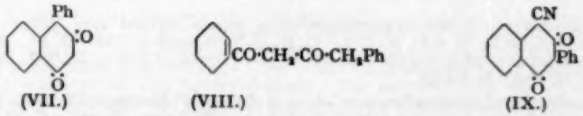
By hydrogenation of the cyanide (I) in alcoholic solution over copper chromite catalyst, we obtained a mixture of two stereoisomeric decahydro*iso*quinolines of general formula (II), in which the *N*-alkyl group is provided by the alcohol used as solvent. In this way, "α"- and "β"-decahydro-1 : 2-dimethyl-4-phenyl*iso*quinoline (II; R = Me), "α"- and "β"-decahydro-2-ethyl-1-methyl-4-phenyl*iso*quinoline (II; R = Et), and "α"- and "β"-decahydro-1-methyl-4-phenyl-2-*n*-propyl*iso*quinoline (II; R = Pr^n) were isolated as colourless oils, and characterised as the corresponding picrates through which salt the separation was achieved by fractional crystallisation. With the *N*-methyl base, the isomers appeared to be present in approximately



equal quantities; but with the *N*-ethyl, and *N*-*n*-propyl derivatives, the isomer giving the picrate of higher melting point seemed to be present in smaller amount. The formation of these bases in two stereoisomeric forms is of some interest as Badger, Cook, and Walker (*J.*, 1948, 2011) isolated only one isomer of the analogous quinoline derivative (IV) after similar hydrogenation of an oxime-ester. On the other hand Barr and Cook (*loc. cit.*) isolated two 1-ethyl-3 : 4-diphenylpiperidines from the products of the reductive cyclisation of ethyl γ-cyano-βγ-diphenylbutyrate. The two isomers of (II) which have now been isolated are possibly *cis* and *trans* with respect to the phenyl and methyl groups.

We also investigated the possibility of synthesising compounds of type (II) by hydrogenation of suitable oxime-esters (*e.g.*, III; compare Badger, Cook, and Walker, *loc. cit.*). Hydrolysis of the cyanide (I) with alcohol and sulphuric acid gave ethyl α-2-acetyl*cyclo*hexylphenylacetate, characterised by alkaline hydrolysis to the acid. All attempts to obtain a crystalline oxime (III) of the ester were unsuccessful, and the crude product was therefore submitted to hydrogenation. The small yield of basic material was fractionally distilled. The first fraction, a colourless oil, was converted into the picrate, which was found to be that of "β"-decahydro-1 : 2-dimethyl-4-phenyl*iso*quinoline. In this case, the product appeared to be homogeneous, and unaccompanied by the "α"-isomer. The second fraction of the distillate which was now insoluble in dilute hydrochloric acid, crystallised, and on fractional recrystallisation was separated into two components. In view of the acid-insolubility, and the fact that reductive cyclisations of this nature are known to proceed *via* the piperidones (Koelsch, *J. Amer. Chem. Soc.*, 1933, **65**, 2093, 2458, 2459, 2460; cf. Barr and Cook, and Badger, Cook, and Walker, *locc. cit.*), these two compounds are regarded as decahydro-3-keto-1-methyl-4-phenyl*iso*quinoline-*A* and -*B* (V). They (V) are presumably formed, during the distillation, by intramolecular cyclisation with loss of the elements of ethanol from the acid-soluble compound (VI). The isomerism is probably of the same nature as that of the compounds of type (II).

It was thought that the keto-ester corresponding to (III) might be more readily available by direct Michael condensation of acetyl*cyclo*hexene and ethyl phenylacetate. In point of fact,

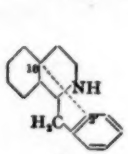


however, a Perkin-type, rather than a Michael-type, condensation was found to be favoured. None of the desired keto-ester was isolated, but two isomeric compounds were separated by fractional crystallisation. The composition of these compounds, which both gave dioximes,

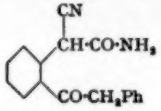
is consistent with the structures (VII) and (VIII), but neither compound gave a colour with ferric chloride.

Similarly, condensation between ethyl cyanoacetate and 1-phenylacetyl*cyclo*hex-1-ene took place by the Perkin rather than by the Michael reaction. In this case only one product was isolated; its composition corresponded with the structure (IX). This compound did not react with carbonyl reagents, but readily formed a *diacetyl* derivative.

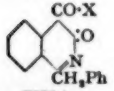
By reactions similar to those described above we have also synthesised a 1-benzyldecahydro-*iso*quinoline (X) which is structurally related to morphinan, the *N*-methyl derivative of which is a potent analgesic (Grewe and Mondon, *Chem. Ber.*, 1948, **81**, 279; Schnider and Grüssner, *Helv. Chim. Acta*, 1949, **32**, 821). In the morphinan structure position 10 of (X) is linked to the 2'-position of the benzene ring, as indicated by the dotted line. Condensation of 1-phenylacetyl*cyclo*hex-1-ene with cyanoacetamide gave α-cyano-α-2-phenylacetyl*cyclo*hexylacetamide



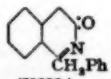
(X.)



(XI.)



(XII.)



(XIII.)

(XI), the amide group of which was hydrolysed by addition of sodium nitrite to a solution of (XI) in hot 50% sulphuric acid. This treatment led also to cyclisation with formation of 1-benzyl-3 : 4 : 5 : 6 : 7 : 8 : 9 : 10-octahydro-3-keto*iso*quinoline-4-carboxylic acid (XII; X = OH), which was obtained more conveniently by hydrolysis of its amide (XII; X = NH_2) prepared directly by condensation of phenylacetyl*cyclo*hexene with malonamide in presence of sodium ethoxide.

The action of nitrous acid on (XII; X = NH_2) gave the corresponding acid (XII; X = OH) which was decarboxylated by heat to 1-benzyl-3 : 4 : 5 : 6 : 7 : 8 : 9 : 10-octahydro-3-keto*iso*-quinoline (XIII). Reduction of this by catalytic hydrogenation over copper chromite was not found possible, but reduction with sodium and dry butanol gave 1-benzyldecahydro*iso*quinoline (X) in satisfactory yield.

Experimental.

α-2-*Acetyl*cyclo*hexylbenzyl Cyanide* (I).—Acetyl chloride and *cyclo*hexene were condensed to give 1-acetyl*cyclo*hex-1-ene by Darzens's method (*Compt. rend.*, 1910, **150**, 709; see also Ruzicka *et al.*, *Helv. Chim. Acta*, 1931, **14**, 1157). The product was characterised as the semicarbazone, m. p. 220° (lit., 220°), and as the *oxime*, the m. p. of which was not in agreement with the published figure. It formed colourless needles, m. p. 61—62°, from aqueous methanol (lit., 90°, 99°), and was unchanged after many recrystallisations (Found: C, 69·3; H, 9·1; N, 9·9. $C_9H_{13}ON$ requires C, 69·1; H, 9·3; N, 10·1%). Acetyl*cyclo*hexene was condensed with benzyl cyanide by the method of Barr and Cook (*loc. cit.*) to give α-2-acetyl*cyclo*hexylbenzyl cyanide, m. p. 119—120°. The *semicarbazone*, prepared in aqueous pyridine, and recrystallised from ethanol, was obtained as small prisms, m. p. 229—230° (decomp.) (Found: C, 68·4; H, 7·4; N, 18·8. $C_{17}H_{22}ON_4$ requires C, 68·5; H, 7·4; N, 18·8%).

*Stereoisomeric Decahydro-2-ethyl-1-methyl-4-phenyl*isoquinolines (II; R = Et).—The above acetyl-*cyclo*hexylbenzyl cyanide (10·4 g.) in ethanol (500 c.c.) was hydrogenated over copper chromite catalyst (3 g.) at 200°/175 atm. for 2 hours. The basic fraction was isolated as a colourless oil (9·0 g.), b. p. 166°/2·5 mm., and was immediately converted into the picrate, and submitted to fractional crystallisation from ethanol.

"α"-*Decahydro-2-ethyl-1-methyl-4-phenylisoquinoline picrate* formed long yellow needles, m. p. 178—179° (Found: C, 59·3; H, 6·4; N, 11·3. $C_{24}H_{30}O_7N_4$ requires C, 59·3; H, 6·2; N, 11·5%). The free *base* was recovered as a colourless oil, b. p. 155°/2 mm. (Found: C, 84·0; H, 10·3; N, 5·4. $C_{18}H_{27}N$ requires C, 84·0; H, 10·5; N, 5·4%).

The "β"-*picrate* formed small yellow needles, m. p. 209—210° (decomp.) (Found: C, 59·5; H, 6·2; N, 11·7%). It gave the free *base* as a colourless oil, b. p. 136°/1 mm. (Found: C, 84·2; H, 10·3; N, 5·5%).

1-*Methyl*-4-*phenyl*isoquinoline.—A mixture of "α"- and "β"-decahydro-2-ethyl-1-methyl-4-phenyl*iso*quinoline (1·5 g.) was dehydrogenated by palladium (0·15 g.) at 300—320°, until hydrogen was

no longer evolved (8 hours). Distillation of the product gave a colourless oil (1·25 g.), b. p. 150—154°/1 mm., which was converted into the picrate. Crystallisation from ethanol and from benzene gave 1-methyl-4-phenyl*iso*quinoline picrate as small yellow needles, m. p. 229—230° (decomp.) (Found: C, 59·2; H, 3·6; N, 12·7. Calc. for $C_{22}H_{16}O_7N_4$: C, 58·9; H, 3·6; N, 12·5%). The free base solidified on storage, and after crystallisation from light petroleum, formed elongated colourless prisms, m. p. 78—79° (Found: C, 88·0; H, 6·1; N, 6·4. Calc. for $C_{16}H_{13}N$: C, 87·7; H, 6·0; N, 6·4%). Krabbe (G.P. 652,041; *Chem. Abs.*, 1938, **32**, 1715) gives m. p.s 206° and 79° for the picrate and free base, respectively.

Stereoisomeric Decahydro-1 : 2-dimethyl-4-phenylisoquinolines (II; R = Me).—Acetyl*cyclo*hexylbenzyl cyanide (10 g.) in methanol (500 c.c.) was hydrogenated over copper chromite catalyst (3 g.) for 4 hours, at 200°/190 atm. The basic fraction was distilled and gave a colourless oil (7 g.), b. p. 150—155°/2 mm., and a non-volatile residue (2 g.). The oil was converted into the picrate, which was then fractionally crystallised from ethanol. *" α "-Decahydro-1 : 2-dimethyl-4-phenylisoquinoline picrate* formed small yellow needles, m. p. 176—177° (Found: C, 58·6; H, 6·1; N, 12·1. $C_{22}H_{22}O_7N_4$ requires C, 58·5; H, 5·9; N, 11·9%). The free *base* was obtained as a colourless oil, b. p. 152°/1·5 mm. (Found: C, 84·0; H, 10·3; N, 5·4. $C_{17}H_{25}N$ requires C, 84·2; H, 10·1; N, 5·7%). The *" β "-picrate* formed long yellow needles, m. p. 205—206° (decomp.) (Found: C, 58·7; H, 5·7; N, 12·1%). The free *base* was obtained as a colourless oil, b. p. 141°/1·5 mm. (Found: C, 84·0; H, 10·1; N, 5·8%).

Stereoisomeric Decahydro-1-methyl-4-phenyl-2-n-propylisoquinolines (II; R = Pr^n).—Acetyl*cyclo*hexylbenzyl cyanide (15 g.) in *n*-propanol (500 c.c.) was hydrogenated over copper chromite (4·5 g.) for 2 hours at 200°/155 atm. The basic fraction was distilled and yielded a colourless oil (15·4 g.), b. p. 173—178°/3 mm. The oil was converted into the picrate, which was then fractionally crystallised from ethanol. *" α "-Decahydro-1-methyl-4-phenyl-2-n-propylisoquinoline picrate* formed yellow needles, m. p. 148—149° (Found: C, 60·0; H, 6·4; N, 11·5. $C_{25}H_{28}O_7N_4$ requires C, 60·0; H, 6·4; N, 11·2%). The *base* was obtained as a colourless oil, b. p. 147—149°/0·8 mm. (Found: C, 83·9; H, 10·3; N, 4·8. $C_{19}H_{29}N$ requires C, 84·1; H, 10·7; N, 5·2%). The *" β "-picrate* formed yellow needles, m. p. 184—185° (decomp.) (Found: C, 60·3; H, 6·2; N, 11·2%). The free *base* was obtained as a colourless oil, b. p. 175° (bath)/0·7 mm. (Found: C, 83·9; H, 10·5; N, 5·0%).

α-2-*Acetyl*cyclo*hexylphenylacetic Acid.*—α-2-Acetyl*cyclo*hexylbenzyl cyanide (4 g.) was hydrolysed by boiling with potassium hydroxide (15 g.) in aqueous ethanol, for 3 hours. The cooled solution was diluted with water (30 c.c.), extracted with ether, acidified with dilute hydrochloric acid, and again extracted with ether. This extract, on evaporation, gave a yellow oil (1·5 g.) which solidified. Crystallisation from light petroleum gave α-2-*acetyl*cyclo*hexylphenylacetic acid* as prisms, m. p. 146—147° (Found: C, 73·7; H, 7·8. $C_{16}H_{20}O_3$ requires C, 73·8; H, 7·7%). A small quantity (0·4 g.) of ether-insoluble material separated when the alkaline reaction mixture was acidified. It crystallised from light petroleum as plates, m. p. 224—225°, and analysis supports its identification as 3 : 4 : 5 : 6 : 7 : 8 : 9 : 10-*octahydro-3-keto-1-methyl-4-phenylisoquinoline* (Found: C, 79·7; H, 8·0; N, 5·9. $C_{16}H_{19}ON$ requires C, 79·7; H, 7·9; N, 5·8%).

As the ester rather than the acid was required for subsequent stages, it was found more satisfactory to carry out the hydrolysis as follows: Acetyl*cyclo*hexylbenzyl cyanide (10 g.) was refluxed for 17 hours with a mixture of 95% ethanol (20 g.) and concentrated sulphuric acid (20 g.). After cooling, the mixture was diluted with water (50 c.c.) and extracted with ether. The extract was washed with dilute aqueous sodium carbonate, dried, and evaporated. The residue, on distillation, gave *ethyl* α-2-*acetyl*cyclo*hexylphenylacetate*, as a colourless oil, b. p. 166—168°/1 mm. (6·0 g.) (Found: C, 75·2; H, 8·3. $C_{18}H_{24}O_3$ requires C, 75·0; H, 8·3%). The identity of this ester was confirmed by its hydrolysis with potassium hydroxide in aqueous ethanol to the acid, m. p. 146—147°, not depressed on admixture with a specimen prepared by direct alkaline hydrolysis of the cyanide.

Hydrogenation of the Oxime (III).—It was not found possible to isolate the pure oxime of the above ethyl acetyl*cyclo*hexylphenylacetate, but a crude specimen was successfully hydrogenated. A solution of the ester (5 g.), hydroxylamine hydrochloride (2·5 g.), and sodium acetate (5 g.) in aqueous ethanol was boiled under reflux for 3 hours. The mixture was poured into water, and the product extracted with ether, to give an oil (5 g.) which did not solidify. A portion of this oil (2·5 g.) in methanol (100 c.c.) was hydrogenated at 200°/145 atm. over copper chromite (1 g.) for 2 hours. The basic fraction was distilled and gave two products, (i) a colourless oil (0·2 g.), b. p. 146° (bath)/1 mm., and (ii) a colourless solid (0·3 g.), b. p. 200—220° (bath)/1 mm. The oil was converted into the picrate which, after crystallisation from ethanol, formed yellow needles, m. p. 202—203° (decomp.), not depressed on admixture with authentic *" β "*-decahydro-1 : 2-dimethyl-4-phenyl*iso*quinoline picrate. The *" α "*-isomer could not be detected. The solid distillate (ii) was separated by fractional crystallisation from light petroleum into two isomers, both of which were insoluble in dilute hydrochloric acid. *Decahydro-3-keto-1-methyl-4-phenylisoquinoline*-A (V) formed small colourless needles, m. p. 180—181°, from light petroleum (Found: C, 79·3; H, 8·5; N, 5·9. $C_{16}H_{21}ON$ requires C, 79·0; H, 8·6; N, 5·8%). The B-*isomer* formed small colourless needles, m. p. 168—169°, from light petroleum (Found: C, 79·0; H, 8·7; N, 5·4%).

*Condensation of Acetyl*cyclo*hexene and Ethyl Phenylacetate.*—A solution of sodium ethoxide (from sodium, 6 g., and ethanol, 120 c.c.) was added slowly to a mixture of 1-acetyl*cyclo*hex-1-ene (30 g.) and ethyl phenylacetate (26 g.). After being heated under reflux for 5 hours, the solution was cooled and poured into 10% hydrochloric acid (375 c.c.). The product solidified overnight, and was collected and washed free from traces of oil with light petroleum. The yellow powder (33 g.) was fractionally crystallised from aqueous ethanol, and separated into two isomeric diketones (VII or VIII ?).

Diketone-A formed small colourless needles (from aqueous ethanol), m. p. 197—198° (Found: C, 79·0; H, 7·5. $C_{16}H_{18}O_2$ requires C, 79·3; H, 7·4%). Microhydrogenation in acetic acid over Adams's platinum catalyst led to hydrogen absorption equivalent to 6·05 double bonds. The *dioxime*, prepared by heating a pyridine solution with hydroxylamine hydrochloride, formed colourless needles (from

aqueous ethanol), m. p. 124—125° (decomp.) (Found : C, 69·6; H, 7·6; N, 9·9. $C_{16}H_{20}O_2N_2$ requires C, 70·6; H, 7·4; N, 10·3%).

Diketone-B, of which about 10 times as much was present in the crude mixture, formed colourless prisms (from light petroleum, b. p. 80—100°), m. p. 169—170° (Found : C, 79·0; H, 7·4%). Micro-hydrogenation led to absorption of hydrogen equivalent to 5·9 double bonds. The *dioxime* formed colourless needles (from aqueous ethanol), m. p. 218—219° (decomp.) (Found : C, 70·6; H, 7·4; N, 9·9%).

Condensation of Phenylacetylcyclohexene with Ethyl Cyanoacetate.—A solution of sodium ethoxide (from 2·5 g. of sodium and 50 c.c. of ethanol) was added slowly to a mixture of 1-phenylacetylcyclohex-1-ene (10 g.; Cook and Hewett, *J.*, 1933, 1106) and ethyl cyanoacetate (5·5 g.). After 4½ hours at room temperature the mixture was poured into 10% hydrochloric acid (180 c.c.). The product solidified overnight, and was washed with a little light petroleum to remove traces of oil. The *compound* [?4-*cyanodecahydro*-1 : 3-*diketo*-2-*phenylnaphthalene* (IX)] crystallised from benzene in colourless prisms, m. p. 199—200° (Found : C, 76·2; H, 6·3; N, 5·0; OEt, 0·0. $C_{17}H_{17}O_2N$ requires C, 76·4; H, 6·4; N, 5·2; OEt, 0·0%).

Like the diketones-*A* and -*B* this substance did not give an appreciable colour with ferric chloride solution. An oxime, semicarbazone, or dinitrophenylhydrazone could not be obtained. Treatment with acetic anhydride in pyridine, for 3½ hours in the cold, gave a *diacetyl* derivative, which crystallised from light petroleum (b. p. 80—100°) in elongated prisms, m. p. 129—130° (Found : C, 72·1; H, 6·0; N, 4·1. $C_{21}H_{21}O_4N$ requires C, 71·8; H, 6·0; N, 4·0%).

1-*Benzyl*-3 : 4 : 5 : 6 : 7 : 8 : 9 : 10-*octahydro*-3-*keto*isoquinoline (XIII).—(*a*) 1-Phenylacetylcyclohex-1-ene (12 g.) was added to a hot solution of malonamide (6·75 g., 10% excess) in dry ethanol (300 c.c.), and then slowly, with stirring, a solution of sodium ethoxide (from 1·7 g. of sodium and 30 c.c. of ethanol). The solution was boiled under reflux for 12 hours, during which some ammonia was evolved, and then evaporated to about 50 c.c. and poured into 10% hydrochloric acid (200 c.c.). After being kept overnight the product was solid and was washed free from oily by-products with a little warm ethanol. Crystallisation from ethanol gave 1-*benzyl*-3 : 4 : 5 : 6 : 7 : 8 : 9 : 10-*octahydro*-3-*keto*isoquinoline-4-*carboxyamide* (XII; X = NH_2) (6·8 g.) as prisms, m. p. 257—258° (decomp.) (Found : C, 71·6; H, 7·0; N, 9·8. $C_{17}H_{20}O_2N_2$ requires C, 71·8; H, 7·0; N, 9·9%).

For hydrolysis to the acid, a solution of sodium nitrite (1 g.) in water (10 c.c.) was slowly added, through a capillary tube below the surface of the liquid, to a solution of this amide (2 g.) in 40% sulphuric acid (130 c.c.) at 100°. The solution was then heated for 5 minutes longer, cooled, and diluted with water (200 c.c.). The solid which separated was dissolved in dilute sodium carbonate solution, and the filtered solution acidified. The precipitated solid was crystallised from benzene giving 1-*benzyl*-3 : 4 : 5 : 6 : 7 : 8 : 9 : 10-*octahydro*-3-*keto*isoquinoline-4-*carboxylic acid* (XII; X = OH) (1·8 g.) as colourless plates (or needles), m. p. 206—207° (decomp.) (Found : C, 71·9; H, 6·2; N, 5·0. $C_{17}H_{19}O_2N$ requires C, 71·6; H, 6·7; N, 4·9%).

For decarboxylation, this acid (1·8 g.) was heated at 210°. Carbon dioxide was freely evolved and after ½ hour the melt resolidified. Crystallisation from ethanol then gave 1-*benzyl*-3 : 4 : 5 : 6 : 7 : 8 : 9 : 10-*octahydro*-3-*keto*isoquinoline (XIII) as colourless needles, m. p. 244—245° (decomp.) (1·3 g.) (Found : C, 80·6; H, 7·1; N, 6·1. $C_{16}H_{19}ON$ requires C, 79·7; H, 7·9; N, 5·8%). The analyses are in better agreement with benzyltetrahydroisoquinolone ($C_{16}H_{17}ON$) which would require loss of hydrogen during decarboxylation. However, the product was insoluble in aqueous sodium hydroxide.

(*b*) To a hot solution of cyanoacetamide (3·5 g., 10% excess) and phenylacetylcyclohex-1-ene (7·5 g.) in dry ethanol (75 c.c.) a solution of sodium ethoxide (from 1·1 g. of sodium and 25 c.c. of ethanol) was added slowly, with stirring. The solution was boiled under reflux for 7 hours, during which evolution of ammonia took place, and was then evaporated to about 50 c.c. and poured into 10% hydrochloric acid (100 c.c.). After being kept overnight, the solid product was washed with a little ethanol to remove oily impurity. *α-Cyano-α-2-phenylacetylcyclohexylacetamide* (XI) (2·2 g.) formed colourless needles (from ethanol), m. p. 247—248° (decomp.) (Found : C, 71·9; H, 7·1; N, 10·1. $C_{17}H_{20}O_2N_2$ requires C, 71·8; H, 7·0; N, 9·9%). The m. p. was strongly depressed on admixture with the isomeric amide (XII; X = NH_2). This cyanide (0·3 g.) was treated with sodium nitrite as described above in the case of the amide (XII; X = NH_2), except that 50% sulphuric acid (50 c.c.) was used and the reaction carried out at 140°. The acid (0·15 g.) obtained had m. p. 206—207° (decomp.), not depressed by a sample prepared as described under (*a*), and the identification was completed by decarboxylation to the same product (XIII).

1-*Benzyldecahydroisoquinoline* (X) (Experiments by G. G. Doig).—The yield of this formed by reduction of (XIII) with sodium and butanol was poor when precautions were not taken to dry the butanol (cf. Koelsch, *J. Amer. Chem. Soc.*, 1943, **65**, 2093). Accordingly, butanol (1 l.) was distilled through a column and the fraction, b. p. 116—117°, was treated with sodium (7 g.), added in small pieces, and then with butyl phthalate (35 g.) (cf. Manske, *J. Amer. Chem. Soc.*, 1931, **53**, 1106). After boiling for an hour, with exclusion of moisture, the solution was distilled through a column and the distillate, protected from moisture, was used for the following reduction : Sodium (1·52 g.) was added to a boiling solution of 1-benzyloctahydro-3-keto*iso*quinoline (XIII) (1 g.) in butanol (20 c.c.). Boiling was continued for ½ hour and the cooled mass was cautiously treated with water (7 c.c.) which dissolved the solid which had separated. The aqueous layer was treated with 2N-hydrochloric acid (20 c.c.), and the butanol was then removed in steam. The residual solution was extracted with ether to remove a trace of coloured material, and then basified and re-extracted with ether. The dried extract, on evaporation, gave crude 1-benzyldecahydro*iso*quinoline (0·7 g.) as a pale yellow oil. It was purified through its oxalate, formed by addition of a solution of oxalic acid (0·02 g.) in dry ether (4 c.c.) to a solution of the base (0·1 g.), also in ether (1 c.c.). The ether was decanted from the precipitated semi-

solid mass, which became completely solid when triturated with ethanol. Crystallisation from dry ethanol gave the *oxalate* of 1-benzyldecahydro*iso*quinoline as colourless microscopic needles, m. p. 230° (decomp.) (Found: C, 74·1; H, 8·9; N, 5·0. $C_{24}H_{44}O_4N_2$ requires C, 74·3; H, 8·8; N, 5·1%). *1-Benzyldecahydroisoquinoline* (X), regenerated from the pure oxalate, was used for the preparation of the following salts. It formed a yellowish liquid, b. p. 135—138°/2 mm. (Found: C, 83·3; H, 10·25; N, 6·3. $C_{16}H_{23}N$ requires C, 83·8; H, 10·1; N, 6·1%).

The *hydrogen tartrate*, prepared from the components in dry ether, formed colourless microscopic rosettes, m. p. 176—177° (Found: C, 63·6; H, 7·4. $C_{20}H_{29}O_8N$ requires C, 63·8; H, 7·7%). The *picrate*, prepared in ethanol, could not be recrystallised on account of dissociation; it formed yellow prisms, m. p. 137° (Found: N, 12·2. $C_{22}H_{24}O_7N_4$ requires N, 12·45%). The *hydrochloride*, obtained by passing dry hydrogen chloride into a solution of the base in dry ether, was dried in a vacuum-desiccator over potassium hydroxide and recrystallised from ethanol. It formed colourless microscopic prisms, m. p. 156—160° (decomp.), which readily took up moisture (Found: C, 72·3; H, 8·5; N, 5·5. $C_{16}H_{24}NCl$ requires C, 72·3; H, 8·7; N, 5·3%).

Our thanks are offered for an I.C.I. Research Fellowship which has enabled one of us (G. M. B.) to take part in this work, and also to the Department of Scientific and Industrial Research for a Maintenance Allowance (to G. M. S. D.). Microanalyses were carried out by Mr. J. M. L. Cameron and Miss R. H. Kennaway.

THE UNIVERSITY, GLASGOW, W.2. [*Received, January 31st*, 1951.]

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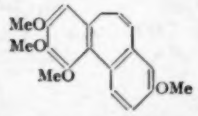
321. *Colchicine and Related Compounds. Part XI. Synthesis of N-Acetylcolchinol Methyl Ether.*

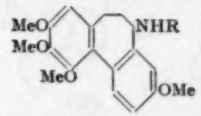
By J. W. COOK, J. JACK, J. D. LOUDON, and (in part) G. L. BUCHANAN and J. MACMILLAN.

Model experiments with 9-methylphenanthrene and with its 2 : 3 : 4 : 5-tetramethoxy-derivative showed that such compounds may be hydroxylated to *cis*-9 : 10-dihydro-9 : 10-dihydroxy-9-methylphenanthrenes. Cleavage of these diols by lead tetra-acetate and cyclisation of the resulting keto-aldehydes afforded the parent dibenz*oxycloheptatrienone* (XII) and its tetramethoxy-derivative (XIX). The process therefore provides a means of synthesising this type of colchicine degradation product.

The trienone (XV), synthesised in this way from 2 : 3 : 4 : 7-tetramethoxy-10-methylphenanthrene, was identical with the ketonic by-product earlier obtained by oxidising deaminocolchinol methyl ether (Part V; Barton, Cook, and Loudon, *J.*, 1945, 176). The isomeric trienone (XXI), synthesised in similar fashion from 2 : 3 : 4 : 7-tetramethoxy-9-methylphenanthrene, was converted, *via* the dienone (XXII) and its oxime, into the primary (±)-amine of the structure proposed for colchinol methyl ether (Part V, *loc. cit.*). Resolution of this amine by means of (+)-6 : 6′-dinitrodiphenic acid afforded the (−)-base and hence its (−)-*N*-acetyl derivatives, which were respectively identical with colchinol methyl ether and its *N*-acetyl derivative as obtained by degradation of colchicine.

IN Part V of this series (Barton, Cook, and Loudon, *J.*, 1945, 176) the structure (I) for deaminocolchinol methyl ether was established on the evidence of degradation and, as one immediate consequence, the conclusion was there reached that formula (II; R = H) represents the most probable structure for colchinol methyl ether. This conclusion has now been confirmed by the synthesis and resolution of the (±)-amine of which the (−)-form and its (−)-*N*-acetyl derivative have proved to be identical with the compounds as obtained by the degradation of colchicine. In the interval between the commencement and completion of our synthetical experiments, other groups of investigators have been attracted to this field and we have been obliged to

(I.) 

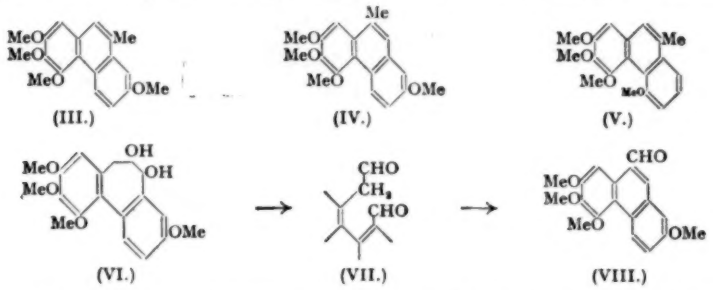


(II.)

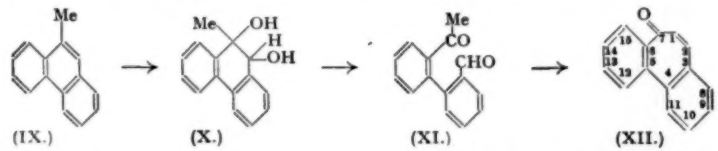
reaffirm our own active interest by publishing two brief announcements of progress (Buchanan, Cook, Loudon, and MacMillan, *Nature*, 1948, **162**, 692; Cook, Jack, and Loudon, *Chem. and Ind.*, 1950, 650) during the course of the work which is here described in full.

Early attempts to synthesise dibenzo*cyclo*heptadienones, *e.g.*, (XXII), from methoxylated β-2-diphenylylpropionic acids having failed for the reasons discussed in Parts VIII and IX (*J.*, 1949, 1079 and *J.*, 1950, 139), attention was turned to methods of expanding the central ring of suitably substituted phenanthrenes. Criegee, Marchand, and Wannowius (*Annalen*, 1942, **550**, 99) showed that their improved procedure for hydroxylating ethylenic bonds is applicable to the 9 : 10-double bond of phenanthrene. The hydrocarbon is thereby converted into *cis*-9 : 10-dihydro-9 : 10-dihydroxyphenanthrene and the process was extended by Cook and Schoental (*J.*, 1948, 170) to the preparation of similar diols from a number of polycyclic aromatic hydrocarbons. Preliminary experiments now showed that a diol is also obtainable by the same means from 9-methylphenanthrene and this opened up the prospect of a flexible synthesis of dibenzo*cyclo*heptatrienones, *e.g.*, (XII), from derivatives of 9- (or 10-)methylphenanthrene by the successive steps of hydroxylation, cleavage, and recyclisation illustrated in the reaction sequence (IX) to (XII).

On these lines the synthesis of degradation products of colchicine requires as starting materials the two isomeric 2 : 3 : 4 : 7-tetramethoxy-9- and -10-methylphenanthrenes, (III) and (IV) respectively. The first of these is already known and like a third isomer, namely (V) which served here for model experiments, was prepared as described in Part IV (Buchanan, Cook, and Loudon, *J.*, 1944, 325) through the corresponding 9-phenanthroic acid. The second isomer, hitherto unknown, was likewise prepared from 2 : 3 : 4 : 7-tetramethoxy-10-phenanthroic acid which was synthesised as described in Part V (*loc. cit.*) and was now converted *via* the hydrazide and phenylsulphonhydrazide into the corresponding 10-phenanthraldehyde and thence into (IV). This 10-phenanthraldehyde (VIII) had already been encountered as a degradation product of colchicine, having been produced (Part V, *loc. cit.*) from deaminocolchinol methyl ether (I), through the intermediates (VI) and (VII), by hydroxylation, cleavage, and recyclisation : samples of the compound from both sources were shown to be identical.

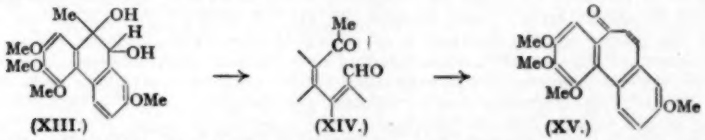


The procedure of Criegee, Marchand, and Wannowius (*loc. cit.*) consists in allowing the compound to be hydroxylated to react with osmium tetroxide in presence of pyridine and generally with benzene as solvent. Thereby the diol is gradually precipitated as a crystalline complex of the osmic ester with pyridine and is liberated by shaking the complex with mannitol in presence of alkali. When applied to 9-methylphenanthrene (IX) this procedure readily afforded the crystalline diol (X) in good yield. Cleavage of the diol was effected by means of lead tetra-acetate and the gummy product, presumably containing the keto-aldehyde (XI), on treatment with sodium hydroxide in methanol afforded 3 : 4-5 : 6-dibenzo*cyclo*hepta-1 : 3 : 5-trien-7-one (XII) which was identical with the compound earlier prepared by the action of selenium dioxide on the parent dibenzo*cyclo*heptatriene (I; H for each OMe) (Part VI, Cook, Dickson, and Loudon,



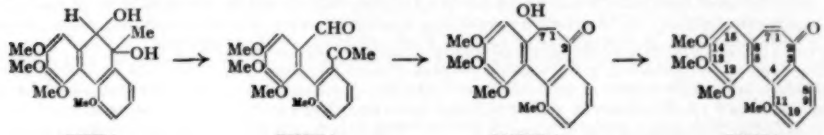
J., 1947, 746). The oxime derived from the trienone (XII), when hydrogenated in acetic anhydride and in presence of Adams's catalyst, was reduced to 2-acetamido-3 : 4-5 : 6-dibenzo*cyclo*hepta-3 : 5-diene (II; R = Ac and H for each OMe).

The yield of (XII) from (X), although somewhat variable, was occasionally very good and appeared to warrant the application of the same procedure to the less accessible tetramethoxy-10-methylphenanthrene (IV). This compound was chosen for investigation at this stage because the product of ring expansion was expected to be identifiable as the unsaturated ketonic by-product obtained from the oxidation of deaminocolchinol methyl ether (I) with chromic acid (Part V, *loc. cit.*). Experiment indeed verified this expectation and the trienone (XV) accordingly becomes the first degradation product of colchicine, for which the central 7-membered ring is established by synthesis. Nevertheless the poor yield obtained made it clear that the discovery of more favourable reaction conditions was a pre-requisite of further progress. The preparation of the diol (XIII) was satisfactory and the process of cleavage appeared to be normal, although again the product was a gum, but cyclisation yielded a mixture of compounds which contained, in addition to (XV), a large proportion of a high-melting solid. While the precise nature of this solid was not ascertained, its properties sufficiently indicated that it was a condensate formed ultimately from two moles of the intermediate (XIV) and therefore at the expense of (XV). It may be interpolated here that this condensate and the unsaturated ketone (XII) are oxidised by sodium dichromate in acetic acid to the corresponding phenanthraquinones and are therefore to be added to the list of compounds which respond to this test of the bridged diphenyl system (cf. Part VI, *loc. cit.*).



(XIII.) (XIV.) (XV.)

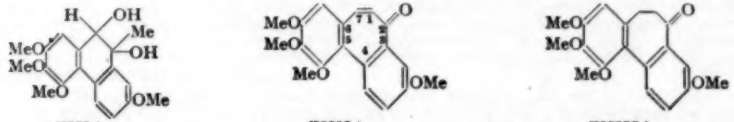
The diol (XVI) obtained by hydroxylating 2 : 3 : 4 : 5-tetramethoxy-9-methylphenanthrene (V) was found to undergo cleavage with the formation of a crystalline keto-aldehyde (XVII) and this facilitated a closer examination of the critical cyclisation stage. When treated with sodium hydroxide in methanol the keto-aldehyde afforded some high-melting solid together with a second product which, from its analysis and its oxidation to 2 : 3 : 4 : 5-tetramethoxyphenanthraquinone, is regarded as the hydroxy-ketone (XVIII). This hydroxy-ketone was the sole product obtained by heating (XVII) with pyridine containing a few drops of piperidine. On attempted acetylation with acetic anhydride in pyridine, the hydroxy-ketone yielded an



(XVI.) (XVII.) (XVIII.) (XIX.)

uncrystallisable gum from which, by distillation, there was obtained the unsaturated ketone (XIX). The latter, however, although still accompanied by some of the hydroxy-ketone, was best prepared by dissolving the keto-aldehyde in acetic acid saturated with hydrogen chloride, and this procedure proved to be most effective for converting (XIV) into (XV), in which case the corresponding hydroxy-ketone was not encountered.

In striking contrast to the other methylphenanthrenes examined here, 2 : 3 : 4 : 7-tetramethoxy-9-methylphenanthrene (III) did not form an insoluble precipitate when treated with



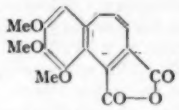
(XX.) (XXI.) (XXII.)

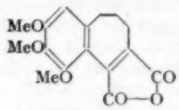
osmium tetroxide in benzene–pyridine. In other respects, however, the reaction appeared to proceed normally and, after a suitable interval, the addition of *n*-hexane afforded an osmic ester from which the diol (XX) was obtained without difficulty. Cleavage by lead tetra-acetate and treatment of the gummy product with acetic–hydrochloric acid yielded the unsaturated

ketone (XXI). This was hydrogenated with palladium as catalyst to the saturated ketone (XXII) the oxime of which, when hydrogenated under pressure with Raney nickel as catalyst, afforded (±)-colchinol methyl ether (II; R = H). The melting points found for the optically inactive base and its immediate derivatives (cf. Cook, Jack, and Loudon, *loc. cit.*) differed markedly from those of the optically active forms which are obtained by degradation of colchicine. They were in fair agreement, however, with the values for corresponding compounds recorded by Rapoport, Williams, and Cisney (*J. Amer. Chem. Soc.*, 1950, **72**, 3324) who in a recent preliminary notice reported a synthesis of (±)-colchinol methyl ether and proved the authentic nature of their product by comparing it with the racemised degradation product.

For the resolution of (±)-colchinol methyl ether, (−)-malic, (+)-tartaric, (+)-camphor-10-sulphonic and (+)-α-bromocamphor-π-sulphonic acids were unsuccessfully tried, although the first two readily afforded crystalline salts. (+)-6 : 6′-Dinitrodiphenic acid, however, proved to be effective, the acid salt of the (−)-base being easily separated from its diastereoisomeride by crystallisation from methanol. By direct comparison of melting points and optical rotations it was shown that the recovered (−)-amine, its salts, and its *N*-acetyl derivative were respectively identical with colchinol methyl ether, its salts, and *N*-acetylcolchinol methyl ether as prepared from colchicine.

It will be observed that this synthesis of *N*-acetylcolchinol methyl ether completes an interesting set of reactions by which the compound is converted into, and is regenerated from, derivatives of phenanthrene. After deamination (II; R = H or Ac) ⟶ (I) (cf. Part V, *loc. cit.*), the process of ring-contraction, (I) ⟶ (VI) ⟶ (VIII), leads to a 9-substituted and ultimately, (VIII) ⟶ (IV), to a 9-methyl derivative of phenanthrene. The contrary, but similarly effected process of ring-expansion, (III) ⟶ (XX) ⟶ (XXI), starts from the isomeric 10-methylphenanthrene and is followed by amination, (XXI or XXII) ⟶ (II). Regarded from a slightly different standpoint these combined processes constitute the interconversion of isomeric 9- and 10-methylphenanthrenes and accordingly would be linked in a continuous reaction-cycle if the lateral nuclei were symmetrically substituted.

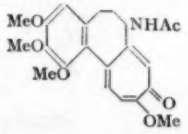
(XXIII.) 

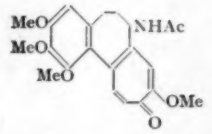


(XXIV.)

In Part X (Cook, Johnstone, and Loudon, *J.*, 1950, 537) it was shown conclusively that the compounds obtained by Windaus by oxidising colchiceine with potassium permanganate were not hydronaphthalene derivatives as he supposed (cf. *Annalen*, 1924, **439**, 59). In particular it was shown that Windaus's *N*-benzoylcolchinic anhydride could be converted into deaminocolchinic anhydride which is quite distinct from the synthesised 6 : 7 : 8-trimethoxy-3-methylnaphthalene-1 : 2-dicarboxylic anhydride and, therefore, like the colchinol derivatives, probably contains the 7-membered ring B, as in (XXIII). This conclusion has recently been substantiated in the synthesis of the dihydride of (XXIII), *viz.*, (XXIV), by Horning and Ullyot and their colleagues (*J. Amer. Chem. Soc.*, 1950, **72**, 4840) of whose work in project we were courteously informed by Dr. G. E. Ullyot. There is consequently good reason to believe that the 7-membered ring B, now established for both the colchinol and colchinic series of degradation products, also occurs in colchicine itself.

Added in Proof.—The recent work of Doering and Knox (*J. Amer. Chem. Soc.*, 1951, **73**, 828) on the transformation of tropolone into tri-iodophenol has now provided a simple counterpart for the change by which ring C of colchiceine becomes phenolic, as in the formation of

(XXV.) 



(XXVI.)

N-acetyliodocolchinol. This provides strong corroboration for the tropolone methyl ether structure of ring C of colchicine. In view of the evidence of structure now provided for compounds of the colchinol type we may conclude that colchicine and *iso*colchicine are correctly formulated as (XXV) and (XXVI), not necessarily respectively.

Experimental.

2 : 3 : 4 : 7-*Tetramethoxy*-10-*phenanthraldehyde* (VIII).—A suspension of 2 : 3 : 4 : 7-tetramethoxy-10-phenanthroic acid (4·5 g.; Part V, *loc. cit.*) in methanol (65 c.c.) and concentrated sulphuric acid (5 c.c.) was heated under reflux for 1 hour and the methyl ester, m. p. (crude) 102°, was recovered from the resulting solution after concentration. The crude ester (5 g.) was heated for 2 hours with 90% hydrazine hydrate (10 c.c.) in ethanol (30 c.c.), thereby yielding the corresponding ***hydrazide*** as platelets of m. p. 216° (from ethanol) (Found : N, 8·0. $C_{19}H_{20}O_5N_2$ requires N, 7·8%). A solution of the hydrazide (4·1 g.) in pyridine (50 c.c.) was treated with benzenesulphonyl chloride (2·1 g.) and, after 12 hours at room temperature, on being poured into dilute hydrochloric acid at 0°, afforded the ***phenylsulphonhydrazide***, m. p. 230—231° (from acetic acid) (Found : N, 5·6. $C_{25}H_{24}O_7N_2S$ requires N, 5·6%). A solution of this compound (5·7 g.; previously dried at 120°) in ethylene glycol (80 c.c.) at 160° was treated with anhydrous sodium carbonate (3·6 g.) and, after 80 seconds, boiling water (100 c.c.) was added. 2 : 3 : 4 : 7-Tetramethoxy-10-phenanthraldehyde was recovered in ether and had m. p. 130° (from methanol), undepressed by admixture with the sample described in Part V (*loc. cit.*) and yielding the same oxime of micro-m. p. and mixed micro-m. p. 164—166°.

2 : 3 : 4 : 7-*Tetramethoxy*-10-*methylphenanthrene* (IV).—The above aldehyde (1·1 g.) was heated for 2 hours with 99% hydrazine hydrate (4 c.c.) in ethanol (40 c.c.). Removal of the solvent afforded a yellow solid of m. p. 145—150°, but this when intimately mixed with powdered potassium hydroxide (2 g.) at 120—125° (oil-bath) readily gave an effervescent melt. Heating was maintained at this temperature for 5—10 minutes, whereafter water was added and the product was recovered in chloroform. 2 : 3 : 4 : 7-*Tetramethoxy*-10-*methylphenanthrene* was conveniently purified by passing its solution in benzene through a column of alumina. It formed colourless prisms, m. p. 134—135°, from benzene (Found : C, 73·2; H, 6·4. $C_{19}H_{20}O_4$ requires C, 73·1; H, 6·4%).

cis-9 : 10-*Dihydro*-9 : 10-*dihydroxy*-9-*methylphenanthrene* (X).—Pyridine (2·4 c.c.) was added to a solution of 9-methylphenanthrene (2 g.) and osmium tetroxide (3 g.) in sodium-dried, thiophen-free benzene (15 c.c.). After 7 days the dark-brown precipitate was collected, dissolved in chloroform and shaken for 2 hours with a solution of mannitol (50 g.) and potassium hydroxide (2 g.) in water (200 c.c.). The yellow chloroform layer was washed and dried and, on evaporation *in vacuo*, afforded the ***diol*** (X) as a gum which crystallised in colourless prisms (1·75 g.) of m. p. 130—131° from methanol–water (Found, after drying for 1 hour at 100°/18 mm. : C, 79·9; H, 6·1. $C_{15}H_{14}O_2$ requires C, 79·7, H, 6·2%).

9-*Methyl*-10-*phenanthrol* was produced when a solution of the diol (X) (0·1 g.) in glacial acetic acid (2 c.c.) and concentrated hydrochloric acid (0·2 c.c.) was briefly heated under reflux (1 minute). It was isolated from the cooled solution by dilution with water and formed almost colourless needles of m. p. 125° from methanol–water (Found : C, 86·2; H, 5·7. $C_{15}H_{12}O$ requires C, 86·5; H, 5·7%). **9-*Methyl*-10-*phenanthryl acetate***, m. p. 150—151° (from methanol–water), was produced when the diol (X) was heated for a short time with acetic anhydride (Found : C, 81·6; H, 5·5. $C_{17}H_{14}O_2$ requires C, 81·6; H, 5·6%).

3 : 4-5 : 6-*Dibenzo*cyclo*hepta*-1 : 3 : 5-*trien*-7-*one* (XII).—A solution of the diol (X) (0·1 g.) in dry benzene (20 c.c.) was treated with lead tetra-acetate (0·21 g.) and the whole was shaken for 2 hours and heated under reflux for ½ hour. The cooled suspension was filtered through charcoal, and the filtrate was washed with water, dried, and concentrated at 40°, affording a colourless gum. This was dissolved in methanol, a drop of dilute sodium hydroxide solution was added and then sufficient water to cause a slight turbidity. The mixture was gently warmed and was set aside for 48 hours under nitrogen in a stoppered tube at room temperature. Usually the trienone (XII) separated in crystalline form and where a gum was obtained this was induced to solidify after chromatography on alumina with benzene as solvent. The trienone formed almost colourless prisms, m. p. 83—85°, from benzene–light petroleum, undepressed on admixture with an authentic sample (Part VI, *loc. cit.*). When heated (½ hour) with sodium dichromate in acetic acid it afforded phenanthraquinone which was isolated as a neutral extract in chloroform from the diluted reaction-liquor and was identified by mixed m. p. and diazine formation.

2-*Acetamido*-3 : 4-5 : 6-*dibenzo*cyclo*hepta*-3 : 5-*diene*.—The ***oxime*** (0·12 g.) of the above trienone (XII), colourless needles, m. p. 190° (from ethanol) (Found : C, 81·8; H, 5·3; N, 6·0. $C_{15}H_{11}ON$ requires C, 81·5; H, 5·0; N, 6·3%), dissolved in acetic anhydride (8 c.c.), was hydrogenated in presence of Adam's catalyst. Absorption was complete in 1½ hours and the ***acetamido*-compound**, obtained by concentration, formed colourless needles, m. p. 233°, from ethanol (Found : C, 81·3; H, 6·9; N, 5·5. $C_{17}H_{17}ON$ requires C, 81·3; H, 6·8; N, 5·6%).

The experiments described above were carried out in conjunction with G. L. Buchanan and J. MacMillan.

On repetition of the preparation of 2 : 3 : 4 : 5-tetramethoxy-9-methylphenanthrene several additions and amendments were noted in respect of the description of the " B-series " of compounds as given in Part IV (*loc. cit.*). In the interval, methyl 2 : 3 : 4 : 5-tetramethoxy-9-phenanthroate—there described as a gum—solidified and, as in the repeated preparation, was readily obtained as colourless plates, m. p. 100°, from methanol (Found : C, 67·15; H, 5·6. $C_{20}H_{20}O_6$ requires C, 67·4; H, 5·6%). From this purer sample of the ester the corresponding hydrazide was obtained with m. p. 193° instead of 182°, the mixed m. p. of the two samples being intermediate.

2 : 3 : 4 : 5-Tetramethoxy-9-phenanthraldehyde as now obtained had m. p. 101° (from ethanol) (Found : C, 69·8; H, 5·5. $C_{19}H_{18}O_5$ requires C, 69·9; H, 5·5%) but a mixture with the beautifully crystalline sample of recorded m. p. 92° again gave this lower value. This is probably another of the numerous cases of polymorphism which have been encountered in these investigations. Still another is found in the case of 2 : 3 : 4 : 5-tetramethoxy-9-methylphenanthrene of which both the original sample —of recorded m. p. 102°—and the new sample were now found to melt at 116—117° (depressed to *ca.* 90° on admixture with 2 : 3 : 4 : 7-tetramethoxy-9-methylphenanthrene, also of m. p. 116—117°), although the lower value had been checked for the original sample on several earlier occasions.

cis-9 : 10-*Dihydro*-9 : 10-*dihydroxy*-2 : 3 : 4 : 7-*tetramethoxy*-10-*methylphenanthrene* (XIII) [with J. MacMillan].—After 14 days at room temperature the pyridine–osmic ester complex from (IV) (0·75 g.) and osmium tetroxide (0·68 g.) in benzene (25 c.c.) and pyridine (1 c.c.) was collected and dissolved in methylene chloride. The filtered solution was shaken with a solution of mannitol (10 g.) and potassium hydroxide (1 g.) in water (100 c.c.) until the organic layer became colourless (1 hour). The gum recovered from this layer afforded the *diol* (XIII) as colourless prisms (0·62 g.), m. p. 155—156°, from methanol–water (Found : C, 66·0; H, 6·4. $C_{19}H_{22}O_6$ requires C, 65·9; H, 6·4%).

9 : 12 : 13 : 14-*Tetramethoxy*-3 : 4-5 : 6-*dibenzo*cyclo*hepta*-1 : 3 : 5-*trien*-7-*one* (XV) [with J. MacMillan].—Lead tetra-acetate (0·08 g.) was added to a solution of the diol (XIII) (0·1 g.) in dry benzene (8 c.c.), and the whole was shaken for 2 hours. The oil (0·085—0·09 g.) recovered from the filtered and washed benzene solution was treated in different experiments in several ways : (*a*) Its solution in methanol was treated with aqueous sodium hydroxide and set aside at room temperature under nitrogen for 3 days. The gummy deposit partly solidified when rubbed with methanol affording a yellow solid (A) and methanol washings. The latter on concentration yielded a gum which was combined with neutral material recovered from the reaction mother-liquor by extraction with chloroform. A solution of these combined gums in benzene was passed through a short column of alumina. Elution of the diffuse yellow band afforded, after recovery, a pale yellow gum which crystallised as yellow sheaves of micro-m. p. 109—111° from ethanol, unchanged on admixture with the ketonic oxidation product of deaminocolchinol methyl ether (Part V, *loc. cit.*). The solid (A) formed cream-coloured needles, micro-m. p. 208—209°, from acetic acid [Found : C, 69·65; H, 6·0%; *M* (micro-Rast), 663; micro-hydrogenation with a palladium catalyst showed absorption of 2 moles of hydrogen]. On oxidation with sodium dichromate in acetic acid this compound gave 2 : 3 : 4 : 7-tetramethoxyphenanthraquinone of micro-m. p. and mixed micro-m. p. 192—194°.

(*b*) Its solution in dry methanol (5 c.c.) was treated with a 5% solution of sodium methoxide in methanol (0·2 c.c.). After 24 hours at 0°, the solution was neutralised with acetic acid, concentrated, and extracted with benzene. Chromatography on alumina gave a yellow band which fluoresced in ultraviolet light and, after elution and recovery, afforded the trienone (0·03 g.), m. p. and mixed m. p. 107—109°.

(*c*) Its solution in glacial acetic acid (5 c.c.) was saturated with dry hydrogen chloride. After 12 hours at room temperature the deep-red solution was diluted with water and extracted with ether. The ethereal extract was washed with sodium hydrogen carbonate solution, then with water, and was dried and concentrated, affording a yellow gum. This solidified when rubbed with methanol, giving the trienone (0·07 g.) of m. p. and mixed m. p. 109—110° (from methanol).

cis-9 : 10-*Dihydro*-9 : 10-*dihydroxy*-2 : 3 : 4 : 5-*tetramethoxy*-9-*methylphenanthrene* (XVI).—After 3 days at room temperature the pyridine–osmic ester complex formed from (V) (0·54 g.) and osmium tetroxide (0·49 g.) in benzene (3·5 c.c.) and pyridine (0·28 c.c.) was collected. Its solution in methylene chloride was shaken as in previous cases with an aqueous solution of mannitol and sodium hydroxide. The recovered *diol* formed colourless needles (0·53 g.), m. p. 215—216°, from methanol (Found : C, 66·1; H, 6·25. $C_{19}H_{22}O_6$ requires C, 65·9; H, 6·4%).

6′-*Acetyl*-6-*formyl*-2 : 2′ : 3 : 4-*tetramethoxydiphenyl* (XVII).—The diol (XVI) (0·2 g.) was cleaved with lead tetra-acetate in benzene as described for (XV). Recovery from benzene gave the *keto-aldehyde* (XVII) as a colourless gum which formed colourless prisms, m. p. 113—114°, from methanol (Found : C, 66·1; H, 5·9; OMe, 35·3. $C_{19}H_{20}O_6$ requires C, 66·25; H, 5·8; OMe, 36%). It yielded a *dioxime*, prisms, m. p. 179—180°, from methanol–water (Found : C, 61·2; H, 5·95; N, 7·7. $C_{19}H_{22}O_6N_2$ requires C, 61·0; H, 5·9; N, 7·5%) and gave no trace of the corresponding phenanthraquinone, being recovered largely unchanged, but with some unidentified acidic product, from oxidation with sodium dichromate in acetic acid.

7-*Hydroxy*-11 : 12 : 13 : 14-*tetramethoxy*-3 : 4-5 : 6-*dibenzo*cyclo*hepta*-3 : 5-*dien*-2-*one* (XVIII).—(*a*) A solution of the keto-aldehyde (XVII) (0·6 g.) in methanol (50 c.c.), treated with a few drops of dilute aqueous sodium hydroxide, gradually deposited (4 days) a high-melting (*ca.* 253°) solid which was discarded. An ethereal extract of the diluted reaction-liquor gave a gum which afforded the *hydroxy-ketone* (XVIII) as colourless needles, m. p. 179—180°, from methanol, either directly or after its solution in benzene had been passed through a column of alumina whereby a first small, yellowish eluate was separated (Found : C, 66·3; H, 6·0. $C_{19}H_{20}O_6$ requires C, 66·3; H, 5·8%). (*b*) The same hydroxy-ketone, m. p. 177—179°, was recovered in ether from a reaction mixture of the keto-aldehyde (0·1 g.) in pyridine (2 c.c.) and piperidine (0·3 c.c.) which had been heated under reflux for 2 hours and then left at room temperature for 2 days before being poured into dilute sulphuric acid at 0°. When oxidised with sodium dichromate in acetic acid the hydroxy-ketone (XVIII) afforded 2 : 3 : 4 : 5-tetramethoxyphenanthraquinone, m. p. and mixed m. p. 123—125° (cf. Part V, *loc. cit.*).

11 : 12 : 13 : 14-*Tetramethoxy*-3 : 4-5 : 6-*dibenzo*cyclo*hepta*-3 : 5 : 7-*trien*-2-*one* (XIX).—(*a*) A solution of the hydroxy-ketone (XVIII) (0·1 g.) in pyridine (0·6 c.c.) was treated with acetic anhydride (0·4 c.c.), and the whole was heated for 1 hour at 100° before being cooled and added to dilute sulphuric acid at 0°. Concentration of a dried ethereal extract yielded an uncrystallisable gum which was distilled at 200° (bath-temp.)/1·5 mm. The distillate when rubbed with methanol afforded the *trienone* (XIX), m. p. 174—175°, from methanol. (*b*) A solution of the keto-aldehyde (XVII) (0·1 g.) in glacial acetic acid (5 c.c.) was saturated with dry hydrogen chloride and, after 12 hours, the resulting red solution was diluted with water. The yellow gum, recovered from an acid-free ethereal extract, was dissolved in benzene, adsorbed on an alumina column and eluted with benzene in two fractions. The first, yellow fraction afforded, after recovery, the trienone (XIX) of m. p. and mixed m. p. with the product from (*a*) 174—175° (from methanol) (Found : C, 69·7; H, 5·7. $C_{19}H_{18}O_4$ requires C, 69·9; H, 5·6%). The second, colourless fraction gave the hydroxy-ketone (XVIII), m. p. and mixed m. p. 179°.

cis-9 : 10-*Dihydro*-9 : 10-*dihydroxy*-2 : 3 : 4 : 7-*tetramethoxy*-9-*methylphenanthrene* (XX).—A solution of (III) (1·3) g. and osmium tetroxide (1·3 g.) in benzene (5 c.c.) and pyridine (0·7 c.c.) after 7 days was red-brown but remained homogeneous. The complex, however, was readily precipitated by the addition of *n*-hexane. It was hydrolysed as described for (XIII), affording the *diol* (XX) as colourless prisms (0·9 g.), m. p. 172—174°, from ethanol (Found : C, 65·9; H, 6·5. $C_{19}H_{22}O_6$ requires C, 65·9; H, 6·4%).

9 : 12 : 13 : 14-*Tetramethoxy*-3 : 4-5 : 6-*dibenzo*cyclo*hepta*-3 : 5 : 7-*trien*-2-*one* (XXI).—The diol (XX) was cleaved with lead tetra-acetate as described in the preparation of the trienone (XV). The cleavage product was a gum which could not be induced to crystallise but reacted with hydroxylamine to form the *dioxime* of 6′-acetyl-6-formyl-2 : 3 : 4 : 4′-tetramethoxydiphenyl, colourless hexagonal plates, m. p. 186—187° (from ethanol) (Found : N, 7·7. $C_{19}H_{22}O_6N_2$ requires N, 7·5%). An attempt to cyclise the gummy cleavage product by means of sodium hydroxide in ethanol yielded only a high-melting solid which was not investigated. Cyclisation was effected in acetic acid saturated with hydrogen chloride as described under section (*c*) for the isomer (XV), affording a gum which was dissolved in benzene and adsorbed on alumina. The resulting yellow band, which fluoresced in ultra-violet light, was preferentially eluted with benzene again affording a gum which, however, slowly solidified yielding the *trienone* (XXI) as yellow prisms, m. p. 98—99° (from methanol) (Found : C, 69·9; H, 5·65. $C_{19}H_{18}O_5$ requires C, 69·9, H, 5·6%).

9 : 12 : 13 : 14-*Tetramethoxy*-3 : 4-5 : 6-*dibenzo*cyclo*hepta*-3 : 5-*dien*-2-*one* (XXII).—The gummy trienone (XXI) was hydrogenated in acetic acid solution in presence of palladium black. The calculated volume of hydrogen (1 mol.) was absorbed in ½ hour and the colourless gum recovered from the filtered solution afforded the dienone (XXII) as colourless prisms, m. p. 142—143°, from methanol (Found : C, 69·5; H, 5·9. Calc. for $C_{19}H_{20}O_5$: C, 69·5; H, 6·1%). It formed an oxime of m. p. 203—204° (from methanol) (Found : C, 66·6; H, 6·4; N, 4·1. Calc. for $C_{19}H_{21}O_5N$: C, 66·4; H, 6·2; N, 4·1%). Rapoport, Williams, and Cisney (*loc. cit.*) who also prepared these compounds report m. p.s 140·5—141° and 194—196° for the dienone and its oxime respectively.

(±)-*Colchinol Methyl Ether* (II; R = H).—This was obtained when the oxime (0·2 g.) mentioned in the last section was hydrogenated at 80—90°/65—75 atm. (4 hours) in methanol (80 c.c.) with Raney nickel. After filtration from the catalyst, the solution was concentrated, water was added, and the base was recovered in dilute sulphuric acid from an ethereal extract. The acid solution was made alkaline and the crude *amine* was obtained by renewed extraction with ether. It formed small colourless rods, m. p. 144—146°, from ether (Found : C, 69·1; H, 7·1. $C_{19}H_{23}O_4N$ requires C, 69·3; H, 7·1%) and when shaken with acetic anhydride in presence of a trace of concentrated sulphuric acid it yielded (±)-N-*acetylcolchinol methyl ether*, m. p. 179—180° (from methanol–water) (Found : C, 67·9; H, 6·9. $C_{21}H_{25}O_5N$ requires C, 67·9; H, 6·8%). The hydrochloride of the (±)-amine had m. p. 254° (decomp.). Rapoport, Williams, and Cisney (*loc. cit.*) do not report the m. p. of the amine but record m. p. 178—179° for the acetyl compound and 258—259° for the hydrochloride.

Resolution of (±)-*colchinol methyl ether*. Solutions of the (±)-amine (0·4 g.) and (+)-6 : 6′-dinitrodiphenic acid (0·4 g.) in methanol (5 c.c. each) were mixed and the resulting crystalline salt (0·364 g.) was crystallised thrice from methanol. [(−)-*Colchinol methyl ether*] [*hydrogen* (+)-6 : 6′-*dinitrodiphenate*] crystallised, with a molecule of methanol, as pale yellow rods, m. p. 257—258° (decomp.), $[\alpha]_{5500}^{16}$ +51°, $[\alpha]_{5461}^{16}$ +67° (*c*, 0·33 in methanol) (Found : C, 58·8; H, 5·05. $C_{19}H_{23}O_4N,C_{14}H_8O_8N_2,CH_4O$ requires C, 58·9; H, 5·1%). The same acid salt, m. p. and mixed m.p. 258° (decomp.), $[\alpha]_{5500}^{16}$ +54°, $[\alpha]_{5461}^{16}$ +69° (*c*, 0·33 in methanol), was prepared from colchinol methyl ether obtained by degradation of colchicine. A solution of the synthesised acid salt (0·2 g.) in methanol was basified by N-sodium hydroxide, and the free base, after recovery in ether, formed very small crystals, m.p. 90—92°, from ether–light petroleum (b. p. 40—60°) and had $[\alpha]_{5500}^{16}$ −85° and $[\alpha]_{5461}^{16}$ −111° (*c*, 0·74 in methanol). An authentic specimen of colchinol methyl ether had m. p. and mixed m. p. 90—92°, $[\alpha]_{5500}^{17}$ −84°, and $[\alpha]_{5461}^{17}$ −111° (*c*, 0·74 in methanol). Samples of the *picrate* of the natural base (prepared by Dr. N. Barton) and of the resolved base had m. p. and mixed m. p. 223—225° (from methanol) (Found : C, 54·1; H, 4·6. $C_{19}H_{23}O_4N,C_6H_3O_7N_3$ requires C, 53·8; H, 4·7%).

N-Acetylcolchinol methyl ether was prepared from resolved synthetic colchinol methyl ether as described for the racemic compound. It crystallised from methanol as colourless prisms, m. p. 202—204°, $[\alpha]_{5500}^{16}$ −92°, $[\alpha]_{5461}^{16}$ −118° (*c*, 0·67 in methanol). An authentic specimen prepared from colchicine had m. p. and mixed m. p. 202—204°, $[\alpha]_{5500}^{17}$ −94°, $[\alpha]_{5461}^{17}$ −118° (*c*, 0·67 in methanol). Rapoport, Williams and Cisney (*loc. cit.*) record m. p. 201—202° and $[\alpha]_D^{20}$ −88·6° (*c*, 0·67 in methanol) for the degradation product.

We are indebted to the Department of Scientific and Industrial Research for Maintenance Allowances (to J. MacM. and J. J.) and to Mr. G. G. Doig for assistance in the preparation of the methylphenanthrenes. Microanalyses were carried out by Miss R. H. Kennaway.

UNIVERSITY OF GLASGOW. [*Received, February 12th*, 1951.]

322. *The Friedel–Crafts Reaction of Fluoranthene.*

By Neil Campbell, W. K. Leadill, and J. F. K. Wilshire.

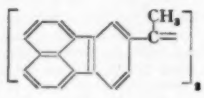
Fluoranthene and acetyl bromide in the presence of aluminium chloride give 4 : 12-diacetylfluoranthene which can be oxidised to fluoranthene-4 : 12-dicarboxylic acid identical with the acid obtained from fluoranthene and oxalyl chloride under Friedel–Crafts conditions (Campbell and Easton, *J.*, 1949, 340).

It has been proved that bromination of fluoranthene gives 4 : 11-dibromofluoranthene (Campbell *et al.*, *Nature*, 1950, **165**, 76; *J.*, 1950, 2784; Holbro and Tagmann, *Helv. Chim. Acta*, 1950, **33**, 2178; S. H. Tucker, personal communication). Nitration, sulphonation, etc., will most probably follow a similar course, but the mode of attack under Friedel–Crafts conditions is less predictable. Von Braun and Manz (*Annalen*, 1932, **496**, 170) showed that the Friedel–Crafts reaction yields 4- and 11-monosubstituted products, but the disubstituted products have never been orientated.

We have therefore investigated the action of acetyl bromide on fluoranthene in the presence of aluminium chloride and find that it yields a mixture of 4- and 11-acetylfluoranthene (I*a* and *b*) which can be separated chromatographically. Both substances on further treatment yield the same diacetylfluoranthene which accordingly must be the 4 : 11- or the 4 : 12-compound. A

(I.)

(I*a*; R = $CO{\cdot}CH_3$, R′ = H.)
(I*b*; R = H, R′ = $CO{\cdot}CH_3$.)
(I*c*; R = R′ = $CO{\cdot}CH_3$.)
(I*d*; R = R′ = CO_2H.)
(I*e*; R = R′ = Br.)



(II.)

decision in favour of the second structure (I*c*) was obtained by oxidation to a fluoranthene-dicarboxylic acid which was different from fluoranthene-4 : 11-dicarboxylic acid prepared from 4 : 11-dibromofluoranthene *via* the dinitrile but identical with the acid obtained by the action of oxalyl chloride on fluoranthene in the presence of aluminium chloride (Campbell and Easton, *loc. cit.*). The Friedel–Crafts product therefore is 4 : 12-diacetylfluoranthene (I*c*), and the derived acid is fluoranthene-4 : 12-dicarboxylic acid (I*d*). This was confirmed by the conversion of the diacetylfluoranthene into the diacetamido-compound by the Schmidt reaction. Hydrolysis followed by diazotisation and the Sandmeyer reaction gave 4 : 12-dibromofluoranthene (I*e*) which was shown to be different from 4 : 11-dibromofluoranthene (Campbell *et al.*, *J.*, 1950, 2784).

It is difficult to say whether in the Friedel–Crafts reactions the 4 : 12-products predominate or not. The fact that considerable purification was required indicates that other isomers are present in quantity, but on the other hand 4-acetylfluoranthene gives a 67% yield of the diacetylfluoranthene.

The acetylfluoranthene prepared by Campbell and Easton (*loc. cit.*) has now been shown to be 11-acetylfluoranthene by conversion into fluoranthene-11-carboxylic acid (Tucker and Whalley, *J.*, 1949, 3213; Campbell and Easton, *loc. cit.*). The acetyl compound undergoes the Schmidt reaction to give 11-acetamidofluoranthene, m. p. 199—201°, previously prepared but not analysed by von Braun and Anton (*Annalen*, 1932, **496**, 191) whose product was not pure since its m. p. was 190°.

Clemmensen reduction of 11-acetylfluoranthene gives a product whose high m. p. suggests that it is not the ethyl derivative but the dimeric 2 : 3-di-11′-fluoranthylbut-2-ene (II) (cf. Steinkopf and Wolfram, *ibid.*, 1923, **430**, 113. Bradlow and Vander Werf, *J. Amer. Chem. Soc.*, 1947, **69**, 1254).

Experimental.

All adsorptions were effected on alumina (Brockmann) and will be described in greater detail in a thesis (Edinburgh) to be submitted by one of us (W. K. L.). Unless otherwise stated, all fluorescence observations were made in ultra-violet light generated by a Hanovia lamp.

Acetylation of Fluoranthene.—Aluminium chloride (36 g., 0·272 mol.) was added to a stirred solution of fluoranthene (20 g., 0·1 mol.) and acetyl bromide (24·6 g., 0·204 mol.) in carbon disulphide (100 ml.) cooled to 0°. The mixture was stirred for 24 hours and then worked up as usual. The product was

shaken with a large volume of ether, and the ether-insoluble portion (17·0 g.) was crystallised first from acetic acid and then from benzene to give a product, m. p. 108—125°. This was dissolved in benzene and chromatographed. Development with benzene–light petroleum gave a lower band (*A*) with a blue fluorescence, an intermediate pale yellow band (*B*), and a top dark yellow band (*C*). *A* gave fluoranthene; the lower part of *B* yielded 4-acetylfluoranthene, m. p. 127—129° (no depression when mixed with an authentic sample), and the upper part gave 11-acetylfluoranthene, m. p. 101—102° either alone or admixed with an authentic sample; and *C* gave diacetylfluoranthene, m. p. 137—139°. Further quantities of these products were obtained by evaporating the acetic acid, benzene, and ethereal filtrates, dissolving the residues in benzene, and separating the constituents chromatographically. Fluoranthene, 4-acetyl-, 11-acetyl-, and 4 : 12-diacetyl-fluoranthene were thus obtained in 17, 2·6, 6·2, and 12·2% yields respectively. By increasing the time of the Friedel–Crafts reaction to 72 hours the respective yields were 1, 4·5, 13, and 37%.

Reactions of 4-*Acetylfluoranthene.*—4-Acetylfluoranthene (0·38 g.) in trichloroacetic acid (2·32 g.) was treated at 60° with sodium azide (0·16 g.) and kept at this temperature for 6 hours. 4-Acetamidofluoranthene (0·2 g.) was isolated by the usual procedure in pale yellow needles, m. p. 244—245° (from acetic acid), with a greenish-yellow fluorescence in the solid state but not in solution (Found : N, 5·5. Calc. for $C_{18}H_{13}ON$: N, 5·4%). This substance (0·15 g.) was boiled with concentrated hydrochloric acid (5 ml.), water (2·5 ml.), and a little ethanol for 20 hours to give 4-aminofluoranthene hydrochloride, m. p. 285°, from which 4-aminofluoranthene was obtained as yellow crystals (from benzene–light petroleum), m. p. 113—115° (lit., 111—112°) (Found : N, 6·3. Calc. for $C_{16}H_{11}N$: N, 6·4%). 4-Acetylfluoranthene dissolves with a strong greenish-yellow fluorescence, and with acetyl bromide gives a 67% yield of 4 : 12-diacetylfluoranthene.

Reactions of 11-*Acetylfluoranthene.*—The acetyl compound with sodium azide and trichloroacetic acid yielded 11-*acetamidofluoranthene*, m. p. 199—201° after crystallisation from benzene (Found : N, 5·2. $C_{18}H_{13}ON$ requires N, 5·4%). 11-Acetylfluoranthene (0·80 g.) in methanol (50 ml.) was slowly added to sodium hypochlorite solution (prepared from 10 g. of sodium hydroxide) kept at 65°. The mixture was stirred at this temperature for 5 hours and the methanol was then removed by distillation. The yellow sodium salt of fluoranthene-11-carboxylic acid (0·41 g.) separated and the filtrate on acidification gave the free acid (0·07 g.). The acid from both sources crystallised from acetic acid in pale yellow needles (0·43 g.), m. p. 284—287° (Found : C, 82·9; H, 4·4. Calc. for $C_{17}H_{10}O_2$: C, 82·9; H, 4·1%). The acid in the solid state has a pale green fluorescence and in solution a blue fluorescence. The methyl ester crystallises in pale yellow needles (from methanol), m. p. 94—97° (Found : C, 82·8; H, 5·0. Calc. for $C_{18}H_{12}O_2$: C, 83·1; H, 4·7%). Both the acid and the ester show no m. p. depression when mixed with authentic samples.

The acetyl compound (2·05 g.) was acetylated as above by acetyl bromide in carbon disulphide in the presence of aluminium chloride. The product was chromatographed on a column 28″ × ¾″ and developed with benzene–light petroleum (3 : 1). The bottom, pale yellow zone yielded unchanged 11-acetylfluoranthene (0·49 g.), and the upper, dark yellow band on elution gave impure diacetylfluoranthene (1·29 g.), m. p. 124—134°, which was purified by further adsorption on a column 16″ × ¾″. 4 : 12-Diacetylfluoranthene (0·61 g.), m. p. 138—142°, thus obtained, showed no m. p. depression when mixed with a sample of the compound prepared as above.

Clemmensen reduction of the acetyl compound (0·72 g.) gave a product which was chromatographed in benzene on a column 20″ × ¾″. Development with benzene–light petroleum (b. p. 80—100°) gave several zones the lowest of which was pale yellow with a yellow fluorescence. This zone on elution yielded a syrup (0·59 g.) which was converted into the picrate (0·08 g.), orange crystals. The picrate in benzene was passed through a column 11″ × ¾″ and development gave a pale yellow band which on elution afforded a product which is probably 2 : 3-*di*-11′-*fluoranthylbut*-2-*ene*, crystallising from ethanol in pale yellow plates (0·2 g.) with a greenish-blue fluorescence, m. p. 272—275° (Found : C, 93·7; H, 5·5. $C_{36}H_{24}$ requires C, 94·7; H, 5·3%).

Reactions of 4 : 12-*Diacetylfluoranthene.*—Diacetylfluoranthene yields, by Brady's method, a *mono*-2 : 4-*dinitrophenylhydrazone*, which was purified by boiling it with ethanol and acetic acid and forms red crystals, m. p. >350°, which sublime in yellow needles (Found : N, 12·0. $C_{24}H_{16}O_4N_4$ requires N, 12·5%). It is probably the 11-compound (cf. Campbell and Easton, *loc. cit.*).

Attempts to reduce the diacetyl compound by the Wolff–Kishner method (Huang-Minlon modification) were unsuccessful, an impure compound containing nitrogen being the only product. Clemmensen reduction gave only unchanged material.

Diacetylfluoranthene (1·0 g.), potassium permanganate (8·7 g.), aqueous sodium carbonate (5 ml.), and water were boiled for 4 hours and yielded 0·60 g. of an acid, m. p. >350°, which was converted into the methyl ester by boiling methanol (20 ml.) and concentrated sulphuric acid (2 ml.) during 20 hours. The ester was purified by dissolving it in benzene and chromatographing the solution. Development with benzene gave a bottom, blue-fluorescing zone which was discarded, and an upper, pale yellow zone with a yellowish-green fluorescence. Elution of this band gave dimethyl fluoranthene-4 : 12-dicarboxylate, yellow elongated prisms (from methanol–acetic acid), m. p. 181·5—183°, not depressed when admixed with the ester prepared by Campbell and Easton (*loc. cit.*) (Found : C, 75·0; H, 4·6. Calc. for $C_{20}H_{14}O_4$: C, 75·5; H, 4·4%).

Chlorine was passed into 100 ml. of an aqueous solution of sodium hydroxide (20 g.) until the solution was neutral to litmus. More sodium hydroxide (5 g.) and water (10 ml.) were added. Diacetylfluoranthene (1·00 g.) was suspended in this solution and was well stirred at 65—70° for 6 hours. The solution was kept overnight, treated with sulphur dioxide, and finally acidified by concentrated hydrochloric acid. Fluoranthene-4 : 12-dicarboxylic acid separated and more was obtained by extraction of the filtrate with ether to give a total yield of 94%.

4 : 12-*Dibromofluoranthene.*—Powdered sodium azide (0·27 g.) was added in two portions at an interval of ½ hour to 4 : 12-diacetylfluoranthene (0·38 g.) in trichloroacetic acid (4·2 g.) kept at 60°. After 8 hours at this temperature the mixture was poured on ice, and the precipitated 4 : 12-*diacetamidofluoranthene* (99%) was washed with water and then boiled with benzene; it had m. p. ~370° (Found : C, 76·0; H, 5·1; N, 8·9. $C_{20}H_{16}O_2N_2$ requires C, 75·9; H, 5·1; N, 8·9%). The compound (0·19 g.) was boiled with concentrated hydrochloric acid (10 ml.) for 2 hours and the solution on cooling deposited greenish-yellow needles of 4 : 12-*diaminofluoranthene dihydrochloride* (88%) (Found : N, 8·9; Cl, 22·8. $C_{16}H_{14}N_2Cl_2$ requires N, 9·2; Cl, 23·2%). Treatment with sodium hydroxide gave the yellow base which, however, was not obtained pure.

The dihydrobromide prepared from diacetylfluoranthene (2 g.) was suspended in 34% hydrobromic acid (20 ml.) and tetrazotised at 0° by 20% aqueous sodium nitrite. The solution was filtered and added slowly to a solution of freshly prepared cuprous bromide (1·1 g.) in 34% hydrobromic acid (3 ml.). The temperature of the mixture was increased during ½ hour to 60° and it was then boiled. The resulting black precipitate was boiled first with chlorobenzene and then with benzene and the combined extracts were passed down a column 12″ × ½″. Development with benzene gave a uniform yellow zone which on elution yielded 4 : 12-*dibromofluoranthene* (0·48 g.), m. p. 162—165° (after crystallisation from benzene) (mixed m. p. with 4 : 11-dibromofluoranthene, 144—152°) (Found : C, 53·4; H, 2·1; Br, 44·7. $C_{16}H_8Br_2$ requires C, 53·4; H, 2·2; Br, 44·4%).

Fluoranthene-4 : 11-*dicarboxylic Acid.*—4 : 11-Dicyanofluoranthene (0·2 g.) was boiled for 3 hours with potassium hydroxide (0·5 g.) in trimethylene glycol (5 ml.). The solution was poured into water, and the precipitate extracted with aqueous sodium carbonate. The extract with dilute sulphuric acid gave *fluoranthene-4* : 11-*dicarboxylic acid* (87%) which sublimed in yellow needles, m. p. >350° (Found : C, 75·2; H, 3·3. $C_{18}H_{10}O_4$ requires C, 74·5; H, 3·6%). The acid was converted by thionyl chloride into the acid chloride and thence into the methyl ester (90 mg.) which was dissolved in benzene and passed through a column 9″ × ¾″. Development with benzene gave a main band, which was yellow and had a yellow fluorescence and on extraction with acetone gave the *dimethyl* ester, bright yellow needles (from methanol), m. p. 168—169°, with a bright yellow fluorescence (Found : C, 74·8; H, 4·3. $C_{20}H_{14}O_4$ requires C, 75·5; H, 4·4%). The ester sublimes in rhombic plates, whereas dimethyl fluoranthene-4 : 12-dicarboxylate sublimes in threads or needles. It gives a big m. p. depression when admixed with this ester.

Thanks are expressed to the Anglo-Iranian Oil Co. Ltd., for a grant, to Imperial Chemical Industries Limited for a grant to one of us (W. K. L.), and to Drs. S. H. Tucker and M. Whalley for a sample of ethyl fluoranthene-11-carboxylate.

UNIVERSITY OF EDINBURGH. [*Received, February 23rd,* 1951.]

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323. *Synthesis of Possible Antimalarials. Part II.* Compounds with the* iso*Quinoline Ring attached to the Quinuclidine System.*

By G. R. CLEMO and S. P. POPLI.

In view of the special interest, both chemical and physiological, attaching to the quinine structure (I) and also to many groups of alkaloids containing the *iso*quinoline system, the synthesis of compounds (II) containing the *iso*quinoline ring attached to the quinuclidine ring of the quinine alkaloids has been attempted.

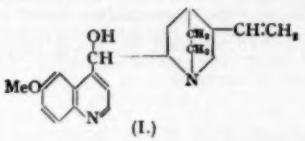
Preliminary experiments showed that ethyl *iso*quinoline-3-carboxylate (III) underwent a normal Claisen reaction with ethyl acetate, although 1 : 2 : 3 : 4-tetrahydro*iso*quinoline-3-carboxylic ester reacted in poor yield; (III) condensed smoothly with ethyl β-(1-benzoyl-4-piperidyl)propionate. On hydrolysis and decarboxylation of the β-keto-ester, 2-4′-piperidylethyl 3-*iso*quinolyl ketone (V) was obtained which, on cyclisation by Rabe's method (*Ber.*, 1931, **64**, 2487), gave 3-*iso*quinolyl 2-quinuclidyl ketone (VI).

SINCE the formulation of the structure of quinine (I) by Rabe (*Ber.*, 1908, **71**, 62) synthetic work has culminated in the syntheses of dihydroquinone (Rabe, Huntenberg, Schulze, and Volger, *Ber.*, 1931, **64**, 2487) and of quinine itself (I) by Woodward and Doering (*J. Amer. Chem. Soc.*, 1944, **66**, 849; 1945, **67**, 860).

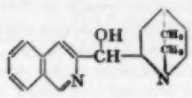
In view of the vast amount of work done in this field and the considerable physiological activity of *iso*quinoline compounds, some of which, *e.g.*, emetine, have a specific action on protozoa, it appeared to be of interest to synthesise and study the antimalarial activity of similar compounds in which the quinoline nucleus was replaced by *iso*quinoline, the simplest of this type being (II). This small variation in structure, while retaining factors which influence

* Part I, *J.*, 1936, 160.

antimalarial activity, should throw some light on the rôle of the quinoline system in the cinchona alkaloids (cf. Work, *J.*, 1940, 1315; 1942, 426) and also the effect of its replacement by *iso*quinoline.



(I.)



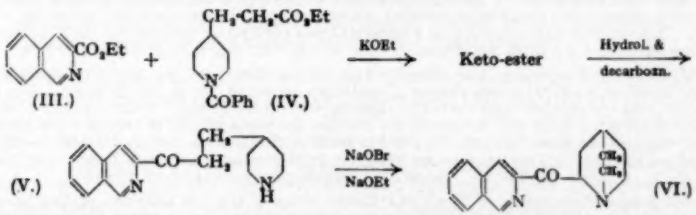
(II.)

Preliminary experiments to this end involved a study of the Claisen condensation on *iso*quinoline-3-carboxylic ester and related compounds. Padbury and Lindwall (*J. Amer. Chem. Soc.*, 1945, **67**, 1268) have prepared methyl 1(and 4)-*iso*quinolyl ketones by a Claisen condensation of *iso*quinoline-1(and 4)-carboxylic esters with ethyl acetate, but no instance of a similar reaction of *iso*quinoline-3-carboxylic ester appears to have been recorded. In view of their observation, which was supported by the independent work of Koelsch (*J. Org. Chem.*, 1945, **10**, 34), who showed that the carbethoxy-group in the 4-position in *iso*quinoline was less active than that in the 1-position, as shown by the respective yields of methyl *iso*quinolyl ketones, and the fact that 1-methyl*iso*quinoline readily condenses with benzaldehyde, whereas 3-methyl*iso*quinoline does not (Mills and Smith, *J.*, 1922, **121**, 2724), it was decided to study the behaviour of ethyl *iso*quinoline-3-carboxylate under comparable conditions. This was prepared from phenylalanine by condensation with formaldehyde by a modification of Pictet and Spengler's method (*Ber.*, 1911, **44**, 2030) and subsequent dehydrogenation of the tetrahydro-ester so obtained with sulphur in tetralin. Palladised charcoal, or choranil (Campbell and Soffer, *J. Amer. Chem. Soc.*, 1942, **64**, 423), was less satisfactory, and although palladium-black gave higher yields, the quantity required would have been prohibitive for large-scale preparative work.

Ethyl *iso*quinoline-3-carboxylate condensed readily with ethyl acetate in the presence of potassium ethoxide in toluene to give the corresponding β-keto-ester. The latter on hydrolysis followed by decarboxylation gave methyl 3-*iso*quinolyl ketone (semicarbazone and phenylhydrazone picrate) in an overall yield of 60%.

A similar condensation of ethyl 1 : 2 : 3 : 4-tetrahydro*iso*quinoline-3-carboxylate with ethyl acetate gave poor yields, which were not improved by using the *N*-benzoyl derivative of the former. In view of this, and the observation that in the cinchona alkaloid series reduction of the quinoline ring increases the toxicity and reduces the antimalarial activity (Boyd, *Amer. J. Hyg.*, 1926, **6**, 173), it was decided to proceed with the dehydrogenated product. Thus, ethyl *iso*quinoline-3-carboxylate behaved similarly to ethyl quininate and related quinoline-carboxylic esters, and from it, therefore, a synthesis of a compound like (II) by Rabe's method appeared possible.

The ethyl β-4-piperidylpropionate required was obtained by catalytic reduction of ethyl pyridine-4-acrylate (Rabe, *Ber.*, 1919, **52**, 1850) with Adams's catalyst in acetic–hydrochloric acid or with Raney nickel at 150°/180 atm. in alcohol, and was then converted into its *N*-benzoyl derivative (IV), which was purified by distillation in a molecular still.



Condensation of (III) and (IV) was effected by heating the mixture of the reactants in toluene with dry potassium ethoxide, the crude intermediate β-keto-ester giving, on hydrolysis with boiling 8N-hydrochloric acid, 2-4′-piperidylethyl 3-*iso*quinolyl ketone (V). This was characterised as its 2 : 4-dinitrophenylhydrazone, dipicrate, and phenylhydrazone dipicrate, and was converted by the action of sodium hypobromite into its *N*-bromo-derivative, which was

cyclised by sodium ethoxide in alcoholic solution to give 3-*iso*quinolyl 2-quinuclidyl ketone (VI). This compound (compare Rabe *et al.*, *loc. cit.*) bears a close resemblance to quininone.

The replacement of the quinoline by the *iso*quinoline residue makes it desirable to test the antimalarial potentialities of (V) and (VI), and the reduction product of the latter in which a secondary alcoholic group unites the *iso*quinoline and the quinuclidine system. This might not only indicate the changes obtained in pharmacological properties by the interchange of the quinoline and *iso*quinoline nuclei, but might also throw some light on the effect of other groups present (*e.g.*, the quinuclidine ring) on the antimalarial activity.

This work is being continued.

Experimental.

Ethyl 1 : 2 : 3 : 4-*Tetrahydroisoquinoline*-3-*carboxylate*.—A mixture of phenylalanine (27·0 g.), methylal (30 ml.), and hydrochloric acid (300 ml.) was left overnight at room temperature and then heated on a steam-bath for 5 hours with occasional shaking, and cooled, and methylal (30 ml.) added. After being kept for another 10 hours at room temperature, the mixture was again heated on a steam-bath for 5 hours and evaporated to dryness under reduced pressure, and the last traces of moisture were removed by adding and distilling off absolute alcohol (25 ml.). Absolute alcohol (150 ml.) was then added, the whole saturated at 0° with hydrogen chloride, left overnight, and refluxed for 3 hours, and the alcohol removed. The residue was basified (K_2CO_3), and extracted thrice with ether, the extract was dried (Na_2SO_4), the solvent removed, and the residue distilled, giving ethyl 1 : 2 : 3 : 4-tetrahydro*iso*quinoline-3-carboxylate as a liquid (12·8 g., b. p. 144—145°/15 mm., 97—98°/0·1 mm.) (Found : C, 70·2; H, 7·7. Calc. for $C_{12}H_{15}O_2N$: C, 70·2; H, 7·3%). Its picrate separated from alcohol as yellow crystals, m. p. 204°.

Ethyl N-*Benzoyl*-1 : 2 : 3 : 4-*tetrahydroisoquinoline*-3-*carboxylate*.—A mixture of the foregoing ester (2·0 g., 0·01 mole) and potassium carbonate (2·8 g., 0·02 mole) in chloroform (10 ml.) was cooled to 0° and an ice-cold solution of benzoyl chloride (1·7 g., 0·012 mole) in chloroform (10 ml.) was added dropwise; the mixture was heated on a steam-bath for 8 hours, then cooled, and the solution filtered, the inorganic salts being washed with chloroform. The combined filtrate and washings were evaporated, the last traces of the solvent being removed in a vacuum, the residue transferred to the molecular still, and the fraction boiling at 150—160° (bath-temp.)/0·0001 mm. collected (2·5 g.) as an odourless, viscous liquid which, on being cooled and touched with ether, solidified; this *benzoyl* derivative had m. p. 79° (Found : C, 73·8; H, 5·9. $C_{19}H_{19}O_3N$ requires C, 73·8; H, 6·1%).

Ethyl iso*Quinoline*-3-*carboxylate*.—A mixture of ethyl 1 : 2 : 3 : 4-tetrahydro*iso*quinoline-3-carboxylate (above) (0·5 g.) and palladium-black (0·35 g.) was heated at 160—170°/25 mm. for ½ hour and distilled, ethyl *iso*quinoline-3-carboxylate (0·35 g.; b. p. 144—145°/0·5 mm.) being obtained (Found : C, 71·4; H, 5·7. Calc. for $C_{12}H_{11}O_2N$: C, 71·1; H, 5·5%). The picrate, m. p. 153°, crystallised from alcohol in yellow needles. Ethyl *iso*quinoline-3-carboxylate was also prepared by dehydrogenation with sulphur in tetralin at 160—165° for 4 hours (Swan, *J.*, 1950, 1536). The yields were, however, lower (25—33%).

Methyl 3-iso*Quinolyl Ketone*.—To a suspension of potassium ethoxide (0·4 g., 0·005 mole) in dry toluene (15 ml.) was added ethyl *iso*quinoline-3-carboxylate (0·65 g., 0·0033 mole), followed by ethyl acetate (0·90 g., 0·01 mole; 100% excess). The brown mixture was heated on a steam-bath for 5 hours and cooled, 8N-hydrochloric acid (15 ml.) was added, and the whole heated on a water-bath for 15 hours and taken to dryness under reduced pressure. The residue was basified (saturated potassium carbonate), extracted with ether, dried (K_2CO_3), and distilled, giving the *ketone* as a pale yellow liquid, which solidified on cooling, and crystallised from light petroleum (b. p. 40—60°) in rectangular plates, m. p. 88° (Found : C, 77·5; H, 5·2. $C_{11}H_9ON$ requires C, 77·2; H, 5·3%); it yielded a *semicarbazone*, rectangular rods, m. p. 216°, from aqueous ethanol (Found : C, 63·4; H, 5·1. $C_{12}H_{12}ON_4$ requires C, 63·2; H, 5·3%), and a *phenylhydrazone picrate*, orange-red needles, m. p. 209°, from ethanol (Found : C, 56·3; H, 3·9. $C_{22}H_{18}O_7N_6$ requires C, 56·3; H, 3·7%).

Ethyl β-4-*Pyridylacrylate*.—β-4-Pyridylacrylic acid (Rabe, *loc. cit.*) (13·5 g.) in absolute alcohol (120 ml.) was saturated with dry hydrogen chloride and warmed on a water-bath for 3 hours. The solvent was removed, and the residue basified (saturated potassium carbonate), extracted with ether, and dried. The residual *ester* solidified on cooling and was purified by sublimation (130°/15 mm.), giving a crystalline solid (11·6 g.), m. p. 64° (Found : C, 68·0; H, 5·9. $C_{10}H_{11}O_2N$ requires C, 67·8; H, 6·2%).

Ethyl β-4-*Piperidylpropionate*.—(*a*) Ethyl β-4-pyridylacrylate (10·0 g.), platinum oxide (100 mg.), and glacial acetic acid (50 ml.) were shaken in hydrogen at 100 lb./sq. in. for 15 hours. The hydrogen was removed, and the catalyst regenerated by shaking with air for ½ hour. Platinum oxide (50 mg.) was added, and shaking continued in hydrogen for another 10 hours at 100 lb./sq. in., the platinum was filtered off, the solvent removed, and the residue basified (50% potassium hydroxide), extracted with ether, dried, and distilled, giving an oily ester (9·1 g.; b. p. 98°/0·1 mm.) (Found : C, 64·8; H, 10·1. Calc. for $C_{10}H_{19}O_2N$: C, 64·9; H, 10·3%); it formed a picrate (from ethanol), m. p. 115°.

(*b*) Ethyl β-4-pyridylacrylate (1·75 g.) and Raney nickel (1·0 g.) in absolute alcohol (75 ml.) were stirred with hydrogen at 150°/180 atm. for 5 hours and worked up as above, giving the reduced compound (1·65 g.).

Ethyl β-(1-*Benzoyl*-4-*piperidyl*)*propionate* (IV).—To an ice-cold solution of the piperidylpropionate (3·3 g.) in chloroform (10 ml.) were added anhydrous potassium carbonate (5·1 g.), and then gradually a solution of freshly distilled benzoyl chloride (2·2 ml.). The mixture was refluxed for 6 hours, the chloroform solution was decanted, the inorganic salts were washed with chloroform, and the combined chloroform solution and washings evaporated to a small volume and transferred to the molecular still.

The fraction, b. p. 145—155°/(bath-temp.)/0·0001 mm., was a thick, colourless, odourless liquid (Found : C, 70·2; H, 8·2. Calc. for $C_{17}H_{23}O_3N$: C, 70·6; H, 8·0%).

2-4′-*Piperidylethyl* 3-iso*Quinolyl Ketone* (V).—To a well-cooled suspension of potassium ethoxide (0·50 g., 0·006 mole) in dry benzene (20 ml.) was added a mixture of ethyl *iso*quinoline-3-carboxylate (1·0 g., 0·005 mole) and ethyl β-(1-benzoyl-4-piperidyl)propionate (1·45 g., 0·005 mole). The mixture was stirred thoroughly and then heated on a steam-bath for 5 hours and cooled, and hydrochloric acid (20 ml.; 4N.) added. The solution was heated on a water-bath for 16 hours and taken to dryness under reduced pressure, the residue basified (saturated potassium carbonate), extracted with ether, and dried, and the solvent removed. The viscous red residue was digested with light petroleum (b. p. 40—60°), and on concentration and cooling gave light cream-coloured crystals which were washed with ether and recrystallised from light petroleum (b. p. 40—60°), giving the *ketone* (150 mg.; m. p. 95°, not raised by further crystallisation) (Found : C, 71·1; H, 8·1. $C_{17}H_{20}ON_2,H_2O$ requires C, 71·3; H, 7·7%); it gave a *dipicrate*, yellow prisms, m. p. 178° (from ethanol) (Found : C, 48·3; H, 3·3. $C_{17}H_{20}ON_2,2C_6H_3O_7N_3$ requires C, 47·9; H, 3·6%). 2 : 4-*dinitrophenylhydrazone hydrogen sulphate*, yellowish-orange, m. p. 250° (decomp.), from alcohol (Found : C, 42·0; H, 4·6. $C_{23}H_{24}O_4N_6,2H_2SO_4,H_2O$ requires C, 41·7; H, 4·5%), and *phenylhydrazone dipicrate*, deep red plates, m. p. 215° (decomp.), from ethanol (Found : C, 51·7; H, 4·4. $C_{23}H_{24}N_4,2C_6H_3O_7N_3$ requires C, 51·7; H, 4·0%).

2-(1-*Bromo*-4-*piperidyl*)*ethyl* 3-iso*Quinolyl Ketone*—The above ketone (116 mg.) was dissolved in N-hydrochloric acid (0·5 ml.) and ether (3·0 ml.), and a solution of bromine (64 mg.) in 6% sodium hydroxide (0·8 g.) added in a fine stream with stirring. The mixture was left for 15 minutes, the ethereal layer separated, and the residue extracted twice with 3 ml. of ether. The combined ethereal extracts were dried (Na_2SO_4) and concentrated to a small volume, and on cooling gave the pure *bromo*-compound (56·0 mg.), m. p. 237° (decomp.) after darkening at 205° (Found : C, 58·6; H, 5·6. $C_{17}H_{19}ON_2Br$ requires C, 58·8; H, 5·5%). Unchanged ketone (22 mg.) was recovered from the sodium sulphate by extraction with boiling ethanol.

3-iso*Quinolyl* 2-*Quinuclidyl Ketone* (VI).—A boiling solution of the *N*-bromo-compound (50 mg.) in ethanol (4·0 ml.) was added to a cold solution of sodium (10 mg.) in ethanol (4 ml.). The brownish-red solution was heated on a water-bath for 30 minutes, allowed to cool, and made slightly acid (dilute hydrochloric acid). The alcohol was distilled off under reduced pressure, the residue basified with sodium hydroxide and extracted with ether, and the ethereal extract dried (Na_2SO_4); on removal of the solvent a viscous liquid was obtained which solidified on cooling. On recrystallisation from light petroleum (b. p. 40—60°), this *ketone* formed crystals (13 mg.), m. p. 85—86° (Found : C, 71·4; H, 7·2. $C_{17}H_{18}ON_2,H_2O$ requires C, 71·8; H, 7·0%).

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324. *The Use of Equilibrium Constants to calculate Thermodynamic Quantities. Part I. Equilibria in the System* tert.-*Butyl Chloride,* iso*Butene, Hydrogen Chloride.*

By K. E. HOWLETT.

Equilibria in the gaseous system *tert.*-butyl chloride–*iso*butene–hydrogen chloride have been measured in the temperature range 61—175°. When hydrogen chloride and *iso*butene are considered as the reactants, the results may be expressed by the formula $\log_{10}K_p = (17{,}700/4{\cdot}575T) - 8{\cdot}27$ (K_p being in atmosphere units). By combining this result with other thermochemical and thermodynamic data, the heat of formation and entropy of *tert.*-butyl chloride are deduced. Comparison of the "experimental" and statistical entropies indicates that the potential barrier to internal rotation is 4·8 kcals./g.-mol. for each methyl group in *tert.*-butyl chloride.

EQUILIBRIA in the gaseous system *tert.*-butyl chloride–*iso*butene–hydrogen chloride were studied by Kistiakowsky and Stauffer (*J. Amer. Chem. Soc.*, **1937**, **59**, 165) and their results may be summarised by the equation $\log_{10}K_p = (17{,}100/4{\cdot}58T) - 7{\cdot}89$, where K_p is in atmosphere units. However, although nominally these measurements were carried out over the temperature range 90—240°, the above result is derived from only 11 experiments, more than half of which lie in a 20° range. For this and other reasons which will appear later, it has seemed desirable to repeat this work.

EXPERIMENTAL.

Material.—Commercial *tert.*-butyl chloride was purified by distillation, the main fraction of b. p. 50·3—50·5° being taken. This product was fractionally crystallised six times. For the last three crystallisations, the f. p. was constant at $-25{\cdot}4° \pm 0{\cdot}1°$ until almost the whole bulk was frozen. The accepted material was dried over calcium chloride plus a little calcium oxide and had the following physical properties : b. p. 50·4°/760 mm., f. p. −25·4°, n_D^{20} 1·3852 ($dn_D/dT = -0{\cdot}00057$).

The vapour pressure of *tert.*-butyl chloride, measured over the range 0—50° with an isoteniscope, may be expressed by the equation

$$\log_{10} p = 32{\cdot}256 - (2596{\cdot}6/T) - 8{\cdot}5055 \log_{10} T$$

whence the Trouton constant is 19·81. (The best recorded values for the principal physical constants have recently been summarised by Barton and Onyon, *Trans. Faraday Soc.*, 1949, **45**, 725.)

Apparatus.—The apparatus is shown diagrammatically in Fig. 1. The Pyrex-glass reactor, which was loosely packed with glass wool [cf. Kistiakowsky and Stauffer, *loc. cit.*, and Rudkowskii and Trifel, *Org. Chem. Ind.* (*U.S.S.R.*), 1936, **2**, 203; *Chem. Abs.*, 1937, **31**, 1004], had a volume of approx. 200 ml., the unheated parts having an estimated volume of 1—2 ml. It was surrounded by a vapour jacket, and was kept at various temperatures by refluxing purified liquids under atmospheric pressure from flask *A*. Determinations of the temperatures with standard thermometers inserted at *B* showed no significant difference at any time from the b. p.s calculated under the prevailing atmospheric conditions. The Bourdon gauge was used as a null-point instrument.

Results.—The equilibria determined have been approached from one side only, namely, by the decomposition of *tert.*-butyl chloride. Equilibrium conditions were indicated by the cessation of pressure changes (cf. Kistiakowsky and Stauffer, *loc. cit.*). Attempts were also made to determine the hydrogen chloride concentration at the completion of reaction, by condensing out the products in a liquid-air trap directly connected to the reactor. The condensate was allowed to warm to room temperature in a current of nitrogen and swept into a Dreschel bottle containing water, as detailed by Barton and Howlett (*J.*, 1949, 155, 165) for ethylene or vinyl chloride–hydrogen chloride mixtures. Subsequent titration of

FIG. 1.

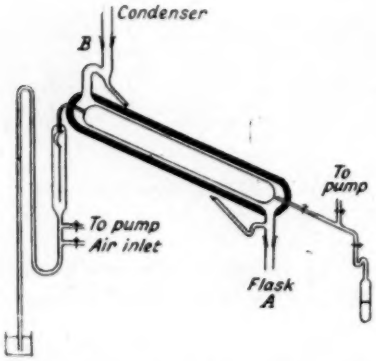
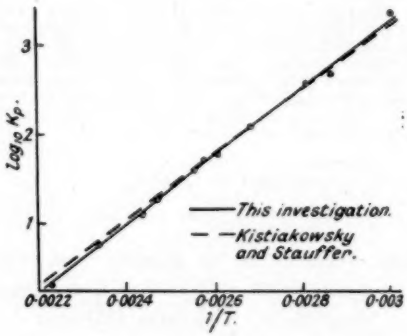


FIG. 2.



the hydrogen chloride with alkali, however, gave variable results for the *tert.*-butyl chloride decompositions, always considerably less than the concentration indicated by pressure measurements. This is not surprising in view of the findings by Kharasch, Kleiger, and Mayo (*J. Org. Chem.*, 1939, **4**, 428) that the rate of the liquid-phase addition of hydrogen chloride to *iso*butene is appreciable at −80° and that it is many times faster than the corresponding addition to vinyl chloride at room temperature.

The reaction was studied at total pressures of between 70 and 200 mm. over the temperature range 61—175°.

It is pertinent to enquire whether pressure gives an accurate measure of concentrations under the stated experimental conditions. The fugacities of hydrogen chloride, *iso*butene, and *tert.*-butyl chloride were therefore calculated from the respective van der Waals constants (see following table, where *a* and *b* are quoted in litre-atmosphere units).

Substance.	*a*.	*b*.	Source.
HCl	3·67	0·0408	Partington, " Advanced Treatise on Physical Chemistry," Vol. I., p. 667.
iso-C_4H_8	12·6	0·109	Calc. from critical data of Beattie, Ingersoll, and Stockmayer, *J. Amer. Chem. Soc.*, 1942, **64**, 546.
tert.-C_4H_9Cl	21·3	0·152	Est. from constants for *iso*butane.

For all these gases up to 1 atmosphere total pressure and over the temperature range covered in these experiments, the fugacities may be expressed as $P - f = xP^2$, where x is a constant for each substance dependent only on the temperature. With P in atmospheres, values of x are as listed below. From these

Temp., ° K.	HCl.	*iso*-C_4H_8.	*tert.*-C_4H_9Cl.	Temp., ° K.	HCl.	*iso*-C_4H_8.	*tert.*-C_4H_9Cl.
323	0·0036	0·0098	0·0187	423	0·0019	0·0041	0·0086
373	0·0027	0·0062	0·0129	473	0·0014	0·0026	0·0064

it is found that the corrections to be applied to pressure measurements are negligible except at the lowest temperatures, where they are of the order of the experimental accuracy (0·1—0·2 mm.). Where necessary, the corrections were applied, and the equilibrium constants obtained are shown below. To facili-

Temp., ° K. ...	334·1	349·9	356·6	373·2	384·0	388·7	392·3	404·8	410·6	428·3	448·2
No. of expts.	2	3	5	5	4	1	1	2	3	7	1
Mean K_p	2590	506	397	127	60·4	54·2	40·8	19·1	12·9	5·97	2·10

tate comparison with the earlier work of Kistiakowsky and Stauffer, K_p is calculated by considering the reaction to be the addition of hydrogen chloride to *iso*butene to give *tert.*-butyl chloride as product.

These results are shown graphically in Fig. 2, where $\log_{10} K_p$ is plotted against the reciprocal of the absolute temperature. The graph obtained by Kistiakowsky and Stauffer is also shown. It will be observed that, though at the lower temperatures the two investigations yield results which are identical within the limits of experimental error, yet at the higher temperatures there is a divergence. Kistiakowsky and Stauffer measured temperatures by means of a thermocouple, whereas in this investigation temperatures have been both calculated from the b. p. of the refluxing liquid at the prevailing atmospheric pressure and observed by the use of standard mercury-in-glass thermometers.

The results of the present investigation may be summarised (by the least-squares method) by the equation

$$\log_{10} K_p = (17{,}700/4{\cdot}575T) - 8{\cdot}27$$

whence $\Delta G^\circ = 17{,}700 + 37{\cdot}8T$, compared with $17{,}100 + 36{\cdot}1T$ obtained by Kistiakowsky and Stauffer.

Discussion.

The heat change derived above, for the dehydrochlorination of *tert.*-butyl chloride, may be combined with other thermochemical data for the heats of formation of *iso*butene and hydrogen chloride, to give the heat of formation of *tert.*-butyl chloride. Thus

$$\Delta Hf^\circ_{390} \text{ for HCl} = -22{\cdot}1 \text{ kcals./g.-mol.}$$

$$\text{and } \Delta Hf^\circ_{390} \text{ for } iso\text{-}C_4H_8 = -4{\cdot}6 \text{ kcals./g.-mol.}$$

(Kilpatrick, Prosen, Pitzer, and Rossini, *J. Res. Nat. Bur. Stand.*, 1946, **36**, 559), whence, if the calculated heat change is taken to refer to the mid-point of the temperature range studied (*viz.*, 390° K.),

$$\Delta Hf^\circ_{390} \text{ for } tert.\text{-}C_4H_9Cl = -44{\cdot}4 \text{ kcals./g.-mol.}$$

This is of particular interest in that the result may be used to obtain a figure for the bond dissociation energy of the carbon–chlorine bond, $D_{CH_3\text{-}Cl}$, in *tert.*-butyl chloride. From ΔHf°_{298} for *tert.*-C_4H_9 = 3·2 (Roberts and Skinner, *Trans. Faraday Soc.*, 1949, **45**, 339), ΔHf°_{390} for *tert.*-C_4H_9 is estimated to be 1·7 kcals./g.-mol., whence

$$D_{(tert.\text{-}C_4H_9\text{-}Cl)} = 75{\cdot}0 \text{ kcals./g.-mol.}$$

This bond dissociation energy may also be calculated by the method suggested by Evans and Polanyi (*Trans. Faraday Soc.*, 1938, **34**, 11) from the corresponding known bond dissociation energy in methyl chloride and the energies of activation for the reactions of sodium atoms with the two halides. Thus, by assuming that $D_{CH_3\text{-}Cl} = 80{\cdot}7$ kcals./g.-mol. (Stevenson, *J. Amer. Chem. Soc.*, 1943, **65**, 209), and that the collision yields for the reactions of sodium with methyl chloride and *tert.*-butyl chloride are respectively 1/7100 at 260° (Heller and Polanyi, *Trans. Faraday Soc.*, 1936, **32**, 633) and 1/1065 at 275° (recalculated from Hartel, Meer, and Polanyi, *Z. physikal. Chem.*, 1932, **19**, *B*, 139), $D_{CH_3\text{-}Cl}$ is calculated from the formula

$$\Delta E_A \text{ for Na} + \text{RCl} = 0{\cdot}27\Delta D_{C\text{-}Cl}$$

to be 74·0 kcals./g.-mol., in good agreement with the figure derived above.

Similarly, knowledge of the entropy change accompanying the reaction allows the calculation of the entropy of *tert.*-butyl chloride. From the experimental equilibrium constant equation, $\Delta S^\circ_{390} = 37{\cdot}82$, and if S°_{390} for HCl = 46·47 (Linnett, *Trans. Faraday Soc.*, 1940, **36**, 527) and S°_{390} for *iso*-C_4H_8 = 76·55 (Kilpatrick and Pitzer, *J. Res. Nat. Bur. Stand.*, 1946, **37**, 163), then S°_{390} for *tert.*-C_4H_9Cl = 85·2.

It is also possible to calculate the statistical entropy of *tert.*-butyl chloride, except for the entropy arising from internal rotations in the molecule. Sheppard (*Trans. Faraday Soc.*, 1950, **46**, 527) has recently given an assignment of the vibrational spectra for the *tert.*-butyl halides. The assigned 33 out of the 36 possible vibrational frequencies of *tert.*-butyl chloride have been grouped for calculation purposes as follows: 304 (2), 372, 406 (2), 570, 811, 917 (2), 950, 1028 (2), 1156, 1237 (2), 1361, 1370 (2), 1450 (6), 2900 (9) cm.$^{-1}$. From these $S^\circ_{\text{vib}\,390} = 11{\cdot}52$. In order to calculate the moment of inertia of the rigid molecule, all interbond angles were assumed to be

tetrahedral and the following dimensions were used: C–C = 1·54 A., C–H = 1·093 A., C–Cl = 1·76 A. Williams and Gordy (*J. Chem. Physics*, 1950, **18**, 994) have shown that the microwave-absorption spectrum is in accord with these assumptions. By using the equation $S_{t+r} = (3R/2)\log_e M + 4R\log_e T + (R/2)\log_e ABC + 265{\cdot}289 - R\log_e 3$, where A, B, and C are the principal moments of inertia of *tert.*-butyl chloride and where the last term arises because the rigid molecule has a three-fold axis of symmetry, the sum of the translational and rotational entropies at 390° K. is found to be 66·95. There is therefore a discrepancy of 6·7$_5$ E.U. at 390° K. between the " experimental " and statistical entropies, which may be ascribed to that arising from the three internal rotations in the molecule. The tables published by Pitzer and Gwinn (*J. Chem. Physics*, 1942, **10**, 430) indicate that the potential barrier restricting rotation of each methyl group is 4·8 kcals./g.-mol. In this evaluation the partition function for free internal rotation was calculated by employing formula 1(*b*) given by Pitzer and Gwinn, in order to take account of the fact that the molecule possesses three tops. If the entropy change in the reaction studied experimentally were as deduced by Kistiakowsky and Stauffer (*loc. cit.*), then the height of the barrier would be 3·0 kcals./g.-mol. Gordon and Giauque (*J. Amer. Chem. Soc.*, 1948, **70**, 1506) have shown by a comparison of statistical and thermal entropies that the barrier restricting the single internal rotation in ethyl chloride is 4·7 kcals./g.-mol. This result is seen to be in better agreement with the entropy found for *tert.*-butyl chloride in the present investigation than that found by Kistiakowsky and Stauffer, since the barrier to rotation per methyl group in *tert.*-butyl chloride would be expected to be at least as high as in ethyl chloride (cf. the values quoted by Pitzer, *J. Amer. Chem. Soc.*, 1948, **70**, 2140, for ethane, propane, and *neo*-pentane).

From the value of S°_{390} and the evaluation of the potential barriers to internal rotation, the standard entropies of gaseous *tert.*-butyl chloride at 25° and at the b. p. are calculated to be 76·06 and 78·35 E.U. respectively.

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325. *Esterification by Dinitrogen Tetroxide.*

By A. D. YOFFE and PETER GRAY.

The reaction at room temperatures between dinitrogen tetroxide and ethyl and methyl alcohol in the liquid and the vapour phase has been examined in outline. Reaction is rapid, and it has been found that very little alkyl nitrate is produced, the products being nitric acid and the alkyl nitrite: $R{\cdot}OH + N_2O_4 \longrightarrow R{\cdot}O{\cdot}NO + HO{\cdot}NO_2$. Oxidation is slight. The importance of this to studies of inflammation of alcohol–nitrogen dioxide mixtures is discussed.

STUDIES of the thermal decomposition in the vapour phase of methyl nitrate (Gray and Yoffe, *Nature*, 1949, **164**, 830; *Proc. Roy. Soc.*, 1949, *A*, **200**, 114) revealed the existence of three distinct modes of reaction, *viz.*, explosive ignition, faintly luminous decomposition, and slow decomposition unaccompanied by light. To obtain information about the behaviour of the nitrates, an investigation was made of the inflammation of gaseous mixtures with dinitrogen tetroxide of the vapours of simple alcohols and aldehydes (*idem*, *J.*, 1950, 3180). It was found that, although mixtures made by adding an excess of dinitrogen tetroxide to alcohol vapour showed the same three modes of reaction as the alkyl nitrate itself, yet mixtures of dinitrogen tetroxide with aldehydes did not exhibit the chemiluminescent reaction. At these temperatures (350°) the oxide is probably reacting as NO_2.

However, it was noticed that when equivalent amounts of methyl alcohol and dinitrogen tetroxide vapours, separately at pressures of about 2 cm., were mixed, decolorization was complete in a few minutes, showing that a rapid reaction was occurring in the cold. The products were all easily condensable and nitric oxide was not found among them by Harris and Siegel (*J. Amer. Chem. Soc.*, 1941, **63**, 2520).

At room temperature nitrogen dioxide and dinitrogen tetroxide exist together in equilibrium and it was thought that the chemical change occurring was not oxidation by

nitrogen dioxide, as at higher temperatures, but esterification by the mixed acid anhydride dinitrogen tetroxide to give both nitrate and nitrite:

$$2R{\cdot}OH + N_2O_4 \longrightarrow R{\cdot}O{\cdot}NO_2 + R{\cdot}O{\cdot}NO + H_2O \quad . \quad . \quad . \quad . \quad . \quad (1)$$

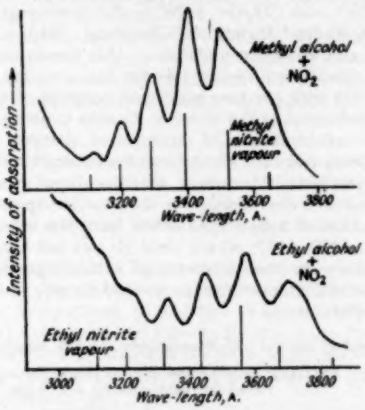
The reaction was therefore carried out both in the gas and in the liquid phase, and the products examined for nitrites and nitrates.

Experimental.

Gas-phase Reaction.—A slight excess of alcohol vapour was mixed in a 4-l. bulb with a few cm. pressure of dinitrogen tetroxide, and reaction allowed to proceed until no brown colour remained. Under these conditions there was a fall of pressure, and at higher concentrations, a mist formed and condensed on the wall.

The mixture was pumped out, condensed in a trap at −170°, and then allowed to warm. It was an acidic liquid and was neutralized with calcium carbonate. During these operations volatile methyl nitrite (b. p. −17°) bubbled off. The residue was examined for methyl nitrate. None was found, and combined nitrogen was not detected by analysis in the fraction distilling below 70°. Nor was ethyl nitrate found among the products of reaction of dinitrogen tetroxide and ethyl alcohol.

Absorption spectra of reaction products (dissolved in ethyl alcohol) compared with absorption spectra of gaseous methyl and ethyl nitrites.



However, both methyl and ethyl nitrites were formed in good yield and were identified spectroscopically by measurements * of light absorption in the wave-length range 2500—4000 A., where the nitrites possess a very characteristic set of maxima in their absorption spectrum (Thompson and Purkis, *Trans. Faraday Soc.*, 1936, **32**, 674; Style, private communication). In the figure the absorption spectra of the reaction products dissolved in ethyl alcohol are compared with the spectra of the gaseous nitrites.

The equation representing the changes occurring is therefore of the form

$$MeOH + N_2O_4 \longrightarrow Me{\cdot}O{\cdot}NO + HNO_3 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2a)$$

Liquid-phase Reaction.—The reaction between ethyl alcohol and dinitrogen tetroxide was also examined in the liquid phase. About 5 ml. of pure liquid dinitrogen tetroxide were distilled into a slight excess of pure ethyl alcohol in a glass tube cooled to −170°. The tube was sealed off and after being allowed to warm gradually to 20° was left for some days. Two layers formed and a pressure above atmospheric was released when the tube was opened. The two layers were separated by cooling and pouring off the upper liquid from the frozen crystals below. On melting, the crystals formed a non-inflammable liquid containing nitric acid.† The upper layer was a pale yellow, odorous, inflammable liquid of low freezing point; it could be distilled below 25°, leaving only a few drops of liquid to distil at 76° with slight charring. It was composed almost entirely of ethyl nitrite (b. p. +17°) though a faint smell of acetaldehyde suggested that very slight oxidation had occurred.

From these experiments it may be inferred that the principal reaction occurring here is

$$EtOH + N_2O_4 \longrightarrow Et{\cdot}O{\cdot}NO + HNO_3 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2b)$$

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* We are grateful to Dr. R. N. Haszeldine for these measurements.

† Whitehurst (private communication) also found nitric acid among the products of this reaction.

Discussion.

The products of the reaction occurring between these simple alcohols and dinitrogen tetroxide in both the gas and the liquid phase are nitric acid and the nitrite ester. The reaction may best be represented by equation (2) and not by (1), since although some aldehyde and nitrate

$$\underset{\text{alcohol}}{ROH} + \underset{\text{mixed anhydride.}}{N_2O_4} \longrightarrow \underset{\text{ester}}{R{\cdot}O{\cdot}NO} + \underset{\text{acid}}{HO{\cdot}NO_2} \quad \ldots\ldots\ldots\ 2)$$

may be formed they are present only in small amounts. [Dinitrogen tetroxide is referred to as a mixed anhydride (nitrous + nitric) although its structural formula is $O_2N{\cdot}NO_2$ and not $ON{\cdot}O{\cdot}NO_2$.] Formally, equations (1) and (2) differ only in the extent to which the reaction $ROH + HO{\cdot}NO_2 \longrightarrow R{\cdot}O{\cdot}NO_2 + H_2O$ has proceeded, and since the equilibrium for this change lies well on the right-hand side, the difference in yields of nitrite and nitrate esters may not be ascribed primarily to the differences in their free energies of formation by these reactions but rather to differences in the activation energies of reactions (1) and (2).

These observations are important to the study of the inflammation of the alkyl nitrates. The initial step in the thermal decomposition of methyl nitrate has been assumed (Appin, Chariton, and Todes, *Acta Physicochim. U.R.S.S.*, 1936, **5**, 655) to be $CH_3{\cdot}O{\cdot}NO_2 \longrightarrow CH_3{\cdot}O^- + NO_2$ (cf. $CH_3{\cdot}O{\cdot}NO \longrightarrow CH_3{\cdot}O^- + NO$ in the decomposition of the nitrite; see, *e.g.*, Steacie, "Atomic and Free Radical Reactions," Reinhold, 1946, p. 141). The $CH_3{\cdot}O$ radical itself gives rise to alcohol and aldehyde molecules; this fission and subsequent reactions of oxidation by the nitrogen dioxide are responsible for the complex behaviour of the nitrates. The glow process is associated with the formation and removal of the $CH_3{\cdot}O$ radicals, and the explosive ignition with the reduction of the nitrogen dioxide to nitric oxide and nitrogen.

Differences between the inflammations of mixtures of nitrogen dioxide with aldehydes on the one hand (2-stage processes) and with alcohols on the other (3-stage processes) are due to the ease with which the latter yield the RO radical, whether directly or through the nitrite ester. In the high-temperature reaction with aldehydes the reactive species is probably NO_2 and its prime reactions the abstraction of a hydrogen atom from the aldehyde giving $R{\cdot}CO$ radicals (McDowell and Thomas, *J.*, 1950, 1462) which yield $R{\cdot}$ but not the $RO{\cdot}$ apparently necessary for luminescence. The nitrite ester itself when mixed with oxygen or with dinitrogen tetroxide shows the same three modes of decomposition as methyl nitrate itself. The table sets out the limits of inflammation of such mixtures.

Spontaneous ignition limit of methyl nitrite–nitrogen dioxide mixtures and related systems.

Temp. 350° c.	Partial pressure (mm. Hg) required for inflammation in hot Pyrex vessel (surface/volume = 0·9 cm.$^{-1}$). Mixture.		
Process.	$MeO{\cdot}NO + NO_2$.	$MeO{\cdot}NO_2 + NO$.	Pure $MeO{\cdot}NO_2$.
Glow	1·4	1·3	0·07
Explosion	2·5	2·2	1·3

The two equimolecular mixtures ($MeO{\cdot}NO_2 + NO$) and ($MeO{\cdot}NO + NO_2$) which yield identical initial products of decomposition (*viz.*, $CH_3O^- + NO + NO_2$ in each case) are seen to behave very similarly.

We express our thanks to Dr. V. M. Clark and to Professor E. D. Hughes, F.R.S., for their comments on the work, to the Ramsay Trust for the award of their Memorial Fellowship (to P. G.), and to the Royal Society for the award of the Mackinnon Studentship (to A. D. Y.).

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326. *The Catalysed Reactions of Simple Aromatic Compounds with Ethylenic Systems. Part I. αβ-Unsaturated Ketones.*

By J. F. J. Dippy and A. L. L. Palluel.

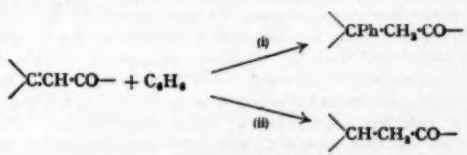
Three distinct processes may occur when an αβ-unsaturated ketone and a benzenoid compound are brought together in the presence of anhydrous aluminium chloride: (i) addition at the ethylenic link, the aromatic residue becoming attached to the β-carbon, (ii) hydrogenation of the ethylenic link, and (iii) replacement of an existing aryl group at the β-carbon of the ketone by an aromatic residue from the benzenoid reactant. Unsaturated ketones used successfully have been benzylideneacetophenone and its nuclear-substituted derivatives, β-phenylcrotonophenone, naphthylacrylophenone, and mesityl oxide, whilst the reactive benzenoid components were benzene, toluene, chlorobenzene, and bromobenzene.

This investigation extends the scope of the results provided by earlier workers, and leads to certain generalisations regarding the effect of the constitution of the unsaturated ketone on the incidence of the above-mentioned processes.

The aluminium chloride is considered to enable the unsaturated ketone to function as an electrophilic reagent for the purpose of aromatic substitution. Molecular compounds of unsaturated ketone and aluminium chloride have been isolated, the constitutions of which are taken into account in the mechanism proposed.

The addition of benzenoid compounds to ethylenic systems in the presence of anhydrous aluminium chloride has long been available as a synthetical method although limited in application. Among the compounds which have received attention have been unsaturated acids and ketones in which the ethylenic link is conjugated with the carboxyl or the carbonyl group.

In the reaction of an αβ-unsaturated ketone with benzene or a suitable monosubstituted benzene, serving as solvent, in the presence of anhydrous aluminium chloride, saturation of the ethylenic link occurs by the alternatives, (i) addition of an aryl group at the β- and hydrogen at the α-carbon atom, or (ii) hydrogenation (the hydrogen atoms being made available by the solvent present in large excess). The nature of the groups contained in the unsaturated ketone seems to determine which process predominates, although in one specific type we have demonstrated that both reactions occur:



The saturated product from either addition will undergo a further reaction (iii) which apparently is slower and leads to the stepwise replacement of aryl groups at the β-position of the ketone by aryl groups supplied by the excess of solvent.

These generalisations rest partly on evidence already recorded. The first such experimental observation appears to have been made by Vorländer and Friedberg (*Ber.*, 1923, **56**, 1144) who added benzene to benzylideneacetophenone; then Hurd (*J. Amer. Chem. Soc.*, 1925, **47**, 2777) showed that benzene and anisole could be added to keten (several such reactions with keten have been reported subsequently). Later, Fuson and his co-workers (*ibid.*, 1934, **56**, 687, 1241, 2103; 1935, **57**, 2208) furnished many instances of aromatic addition, accompanied by replacement, in αβ-unsaturated ketones, and claimed that both processes were reversible. The following kind of observation has been made in many cases:

$$C_6H_5\cdot CH{:}CH\cdot COR \xrightarrow{2C_6H_5X} (X\cdot C_6H_4)_2CH\cdot CH_2\cdot COR$$

$$X\cdot C_6H_4\cdot CH{:}CH\cdot COR \xrightarrow{2C_6H_6} (C_6H_5)_2CH\cdot CH_2\cdot COR$$

In a similar reaction involving benzene and *p*-bromobenzylidenequinaldine, bromobenzene was identified as a product (Fuson *et al.*, *ibid.*, 1933, 55, 3799) but the fates of displaced groups in reactions of αβ-unsaturated ketones have not been established as yet. The replacement process (iii), implicit in the above reactions, involves aryl groups only: where alkyl groups occupy the β-position the change is not observed. It is noteworthy that replacement of R, which occupies a terminal position adjacent to carbonyl, does not occur, whether it be alkyl or aryl. Our investigation reinforces and extends these conclusions, and the recent work of Colonge and Pichat (*Bull. Soc. chim.*, 1949, Jan., p. 177; May, p. 142) also gives valuable confirmation of several features. These authors showed, for instance, that in aluminium chloride-catalysed reactions of benzene, toluene, and anisole with methyl ketones containing alkyl-substituted vinyl groups, addition occurred at the β-position and along customary lines (often giving very good yields), but there was no case where subsequent replacement took place.

The incidence of addition process (i) or (ii) seems to be confined to specific categories of unsaturated ketones. Thus in the system CR′R″:CH·CO· where R′ and R″ are H–H, alkyl–H, alkyl–alkyl, or aryl–H, process (i) occurs exclusively. On the other hand process (ii), *i.e.*, exclusively hydrogenation, takes place in the system where both R′ and R″ are aryl (Fuson *et al.*, *loc. cit.*). A position intermediate between these extremes is represented by the system in which R′ = alkyl and R″ = aryl, as we have shown that dypnone, CPhMe:CH·COPh, undergoes both kinds of reaction concurrently. It would appear from the above that, as the bulk of the group situated at the β-position increases, the hydrogenation process is favoured at the expense of the other addition process, so much so that where R′ and R″ are represented by two aryl groups the addition of a further aromatic nucleus to the β-position is so inhibited as to become negligible. Of course, bulk is not likely to be alone responsible, as changes in groups are accompanied by changes in polar influences.

An interesting reaction is provided by the addition of benzene to cinnamylideneacetophenone; this gives ββδ-triphenylvalerophenone, *i.e.*, two benzene molecules have added across the ethylenic bonds of the unsaturated ketone.

The effect of changing the character of the benzenoid reactant (always a liquid and in large excess) has also been examined by us. We found that apart from benzene, the liquids toluene, chlorobenzene, and bromobenzene gave addition; no success was met when anisole, nitrobenzene, ethyl benzoate, or pyridine was used, and iodobenzene and dimethylaniline underwent independent chemical changes under the standardised experimental conditions.

The orienting influence of the substituent in the benzenoid compound is significant; in successful additions and replacements the *p*-position of the entering ring is the point of attachment. A striking claim is that of Fuson and his co-workers (*loc. cit.*) who record that chlorobenzene reacts with *m*-chlorobenzylideneacetophenone to give ββ-di-*p*-chlorophenylpropiophenone. It is interesting, however, that when we treated the same ketone with unsubstituted benzene the addition reaction alone took place.

Our experimental procedure approximates to that described by Shildneck (*Org. Synth.*, **17**, 51—53) although in the first place we examined a number of factors which might have called for modification. We confirmed that the optimum proportion of catalyst was 2—2·5 mols. (with respect to the ketone) except in one case. The introduction of dry hydrogen chloride was not generally found necessary or advantageous; moreover, raising the temperature was without effect, every successful reaction proceeding at room temperature. We, also, showed that stannic chloride, a weaker electron acceptor, was of no catalytic value, and in this connexion it is significant that Colonge and Pichat (*loc. cit.*) found boron trifluoride ineffective in their work.

Unsaturated ketone.	Benzenoid compound.	Products.
CMe_2:CH·COMe	PhCl	*p*-C_6H_4Cl·CMe_2·CH_2·COMe
CHPh:CH·COPh	PhMe	(*p*-$C_6H_4Me)_2CH$·CH_2·COPh
,,	PhCl	*p*-C_6H_4Cl·CHPh·CH_2·COPh & (*p*-$C_6H_4Cl)_2CH$·CH_2·COPh
,,	PhBr	*p*-C_6H_4Br·CHPh·CH_2·COPh
m-C_6H_4Cl·CH:CH·COPh	C_6H_6	*m*-C_6H_4Cl·CHPh·CH_2·COPh
CPhMe:CH·COPh	C_6H_6	CHPhMe·CH_2·COPh & CPh_2Me·CH_2·COPh
CHPh:CH·CH:CH·COPh	C_6H_6	$CHPh_2$·CH_2·CHPh·CH_2·COPh
β-$C_{10}H_7$·CH:CH·COPh	C_6H_6	$CHPh_2$·CH_2·COPh

The annexed table summarises our results. The entry of aryl groups at the β-position relative to carbonyl in αβ-unsaturated ketones has been demonstrated experimentally in some cases (Fuson *et al.*, and Colonge and Pichat, *locc. cit.*) by oxidative degradation. Moreover,

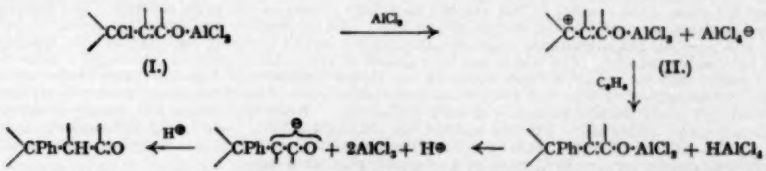
certain of the products, *e.g.*, benzylacetone, obtained in Colonge and Pichat's work possessed constitutions which were beyond doubt. For ββ-di-*p*-chlorophenylpropiophenone and 4 : 4-di-*p*-chlorophenylbutan-2-one, we have confirmed the β-orientation by oxidation with alkaline permanganate; we have simultaneously proved attachment at the *p*-position in the case of reactions with chlorobenzene, since in both cases *pp'*-dichlorobenzophenone was produced. Furthermore, benzophenone was formed in the oxidation of ββδ-triphenylvalerophenone.

In the reaction of naphthylacrylophenone with benzene to give ββ-diphenylpropiophenone, a high-boiling liquid residue recovered from the excess of benzene doubtless contained the displaced naphthyl group. It had an odour reminiscent of that of naphthalene but no solid component was recovered, and attempted conversion into a picrate was unsuccessful, signifying that aluminium chloride had reacted further with the naphthalene residue.

In the case of benzylideneacetophenone the reaction with chlorobenzene was arrested at the addition stage, *i.e.*, to give β-*p*-chlorophenyl-β-phenylpropiophenone. The second stage was reached by further treatment of the product, and it is noteworthy that whilst the first stage takes five hours, the second stage requires seventeen hours for completion.

In all experiments, whether addition occurred or not, there was always darkening of the liquid mixture and as a rule a light-coloured solid was formed. In two cases these solids have been isolated, and analyses show them to be equimolecular compounds of the unsaturated ketone with aluminium chloride. After storage they react to completion with the benzenoid solvent, although only after introduction of one further molecular proportion of aluminium chloride; thus it seems that the formation of a binary complex with the unsaturated ketone is not the sole function of the catalyst (it had already been found that 2—2·5 moles of aluminium chloride was essential for the success of reactions conducted without interruption). The 1 : 1 molecular composition of the complex in the case of cinnamylideneacetophenone points to the association of aluminium chloride with the carbonyl group rather than with the ethylenic linkage exclusively. It is noteworthy that lately Dilks, Eley, and Sheppard (*Trans. Faraday Soc.*, 1950, **46**, 261) have also demonstrated the 1 : 1 composition of some compounds of simple ketones with aluminium chloride (see also Thomas, "Anhydrous Aluminium Chloride in Organic Chemistry," 1941, pp. 50 and 51).

To account for the observed facts we submit that the co-ordination product $\rangle\overset{\oplus}{C}\cdot\underset{|}{C}:\underset{|}{C}\cdot O\rightarrow\overset{\ominus}{A}lCl_3$, formed initially, gives the structure $\rangle CCl\cdot\underset{|}{C}:\underset{|}{C}\cdot O\cdot AlCl_2$, by intramolecular rearrangement, a process favoured by the spatial considerations. Such a compound will require a further proportion of aluminium chloride in order to participate in an orthodox Friedel–Crafts reaction. Thus we favour the following mechanism for the addition process (i), as accounting best for the experimental observations:



The mechanism is thus one of initial production of a carbonium cation (II) in the aprotic solvent-reagent (in the case of cinnamylideneacetophenone the cation is mesomeric). It is recognised, however, that the second aluminium chloride molecule with hydrogen chloride, inevitably generated during reaction, would give rise to proton which is also effective in removing chlorine from the initial binary complex (I) to given the carbonium ion (II). The lack of reactivity of nitrobenzylideneacetophenone (even with four molecular proportions of aluminium chloride), observed by us, is apparently caused by the inhibition of reaction between the binary complex and the second molecule of aluminium chloride, *i.e.*, the chlorine in the complex is held so firmly, in consequence of the strong electron attraction of nitroxyl ($-I$, $-T$), as to inhibit the formation of the carbonium cation.

We recognise that the mechanism advanced here for unsaturated ketones is a specific one, and cannot apply to similar additions involving alkenes, unsaturated acids, etc., which are known also to occur under Friedel–Crafts conditions; these are to be the subject of further inquiries.

It should be appreciated that the addition reactions discussed in this paper can be regarded

as special instances of the Michael-type condensation in which the catalyst is acidic. Hauser and Breslow (*J. Amer. Chem. Soc.*, 1940, **62**, 2385) have claimed that their successful addition of ethyl malonate to ethyl benzylidenemalonate under the influence of boron trifluoride was the first example of an acid-catalysed Michael addition, but strictly speaking many instances were already known (in the sense described in this paper), some of the earliest being provided by Liebermann and Hartmann (*Ber.*, 1891, **24**, 2582; 1892, **25**, 957, 2124), Karsten (*Ber.*, 1893, **26**, 1579), and Eijkman (*Chem. Weekblad*, 1908, **5**, 655) who caused aromatic hydrocarbons to react with cinnamic acid under the influence of sulphuric acid or anhydrous aluminium chloride.

The mechanism advanced by Colonge and Pichat (*loc. cit.*) for the addition of benzenoid compounds to aliphatic unsaturated ketones involves initial addition of hydrogen chloride to the ethylenic link to give a saturated β-chloro-ketone; this is essentially the view advanced originally by Vorländer and Friedberg (*loc. cit.*). Presumably this implies electrophilic addition, a process which would be much inhibited by the neighbouring carbonyl group. It is true that Colonge and Pichat were able to make saturated ketones from such β-chloro-ketones by treatment with benzene and aluminium chloride, but this does not prove that saturated β-chloro-ketones are an essential step where the unsaturated ketone is used as starting material. We prefer to follow the principle that the system $>C{:}C\cdot C{:}O$ is essentially attractive to nucleophilic reagents.

In this connexion it is noteworthy that in Colonge and Pichat's experiments attachment of benzene seems to occur less readily when methyl groups occupy the β-position, partially satisfying thereby the electron deficiency at that carbon atom.

In conclusion it is interesting that recently addition between benzene and acetylenic ketones under the influence of sulphuric acid has also been effected (Bickel and Fabens, *J. Amer. Chem. Soc.*, 1949, **71**, 1450).

A far better knowledge of the factors governing the replacement reaction, as distinct from the addition process, will be needed before an interpretation can be undertaken, and work on this matter involving unsaturated ketones, nitro-compounds, and carboxylic acids is in progress.

Experimental.

Unsaturated Ketones.—The benzylidene-ketones were prepared by the condensation of the aldehyde with the appropriate methyl ketone in the presence of 10% aqueous alcoholic sodium hydroxide.

In the condensation of β-naphthaldehyde and acetophenone in equimolecular proportions a very low concentration of sodium hydroxide was used in order to preclude the Cannizzaro reaction which this aldehyde so readily undergoes, as for instance with the 10% alkali solution. *β-2-Naphthylacrylophenone* recrystallised from alcohol in fine, colourless needles, m. p. 157—158° (yield, 60%) (Found: C, 87·4; H, 5·2. $C_{19}H_{14}O$ requires C, 88·3; H, 5·4%).

Reactions of Benzenoid Compounds with Unsaturated Ketones.—A solution of the unsaturated ketone in the benzenoid solvent was added gradually to a cooled suspension of anhydrous aluminium chloride (about 2·2 mols. with respect to the ketone) in a large excess of the same solvent. The temperature of the mixture was not allowed to rise above 20°. The suspension was stirred at room temperature until the precipitated aluminium chloride–unsaturated ketone complex had passed into solution and for 1 hour subsequently. The whole was then added to hydrochloric acid–ice, the organic layer washed with water, and excess of solvent removed by steam-distillation. The resultant crude crystalline product obtained on storage was often contaminated by gum (doubtless arising from polymerisation); much of this could usually be removed on a porous tile. Recrystallisation was usually effected from aqueous alcohol (charcoal). By this method we obtained a 78% yield of *ββ*-diphenylpropiophenone (m. p. 91—92°) from the benzene–benzylideneacetophenone reaction; under similar conditions benzylideneacetone gave a 70% yield of **4**: 4-diphenylbutan-2-one.

Two modifications of the above procedure—in one the aluminium chloride suspension is saturated with dry hydrogen chloride before addition of the unsaturated ketone, and in the other powdered aluminium chloride is added to a hydrogen chloride-saturated solution of the ketone—did not improve the yields or decrease the amount of gum.

Throughout our experiments it was generally found that where reaction failed to take place at room temperature and with 2·2 mols. of catalyst, the use of forcing conditions, *e.g.*, a higher proportion of catalyst and an elevated temperature, was also unavailing.

Details relating to the separate systems are as follows: *Mesityl oxide and chlorobenzene.* The intermediate complex did not separate as a solid, and the reaction was allowed to proceed for approximately 30 hours, whereupon a dark brown colour developed. The product was separated, together with the excess of solvent, by steam-distillation and was recovered as an oil (yield 62%); from it *4-p-chlorophenyl-4-methylpentan-2-one semicarbazone* was prepared, crystallising from alcohol in colourless leaflets, m. p. 174—175° (Found: Cl, 12·7. $C_{19}H_{14}ON_3Cl$ requires Cl, 13·2%).

Benzylideneacetophenone and toluene. The residue from the ethereal extract of the crude reaction product (stirring for 2½ hours was needed) gave a paste when left in a vacuum-desiccator for 2 days. This paste, after being pressed on porous porcelain, crystallised from alcohol (charcoal) as fine needles, m. p. 77—78°, and is considered to be *ββ-di-p-tolylpropiophenone* (yield 28%) (Found: C, 87·5; H, 7·0. $C_{23}H_{22}O$ requires C, 87·9; H, 7·0%).

Benzylideneacetophenone and chlorobenzene. This reaction was arrested by pouring the reaction mixture into dilute hydrochloric acid after 5 hours. *β*-p-*Chlorophenyl-β-phenylpropiophenone* was recovered in the usual way and recrystallised from aqueous alcohol as colourless needles, m. p. 92—93° (yield 32%) (Found: C, 77·8; H, 5·5; Cl, 11·2. $C_{21}H_{17}OCl$ requires C, 78·6; H, 5·3; Cl, 11·1%).

When the reaction mixture above was given prolonged stirring (17 hours in all) the product was *ββ*-di-*p*-chlorophenylpropiophenone, m. p. 120—121° (59% yield) (previously obtained by Fuson *et al.*, *J. Amer. Chem. Soc.*, 1934, **56**, 687, with m. p. 120—121°). Oxidation of this product with alkaline permanganate (5 hours) gave *pp'*-dichlorobenzophenone, m. p. 143—144°, in good yield.

A similar oxidation of 4 : 4-di-*p*-chlorophenylbutan-2-one, obtained by the reaction of chlorobenzene with benzylideneacetone, also gave *pp'*-dichlorobenzophenone.

Benzylideneacetophenone and bromobenzene. The product, recovered after 7 hours' stirring, was regarded as *β*-p-*bromophenyl-β-phenylpropiophenone.* It recrystallised from aqueous alcohol in colourless needles, m. p. 105—106° (yield, 50%) (Found: C, 69·3; H, 4·7; Br, 21·2. $C_{21}H_{17}OBr$ requires C, 69·0; H, 4·7; Br, 21·9%). A similar reaction, allowed to continue for 50 hours, yielded an impure product which gave indications of being an intractable mixture of the mono- and di-bromo-substituted saturated ketones.

m-*Chlorobenzylideneacetophenone and benzene.* Addition of dry hydrogen chloride was found advantageous in this experiment. The yellow solid intermediate did not dissolve even after 21 hours' stirring at room temperature and subsequent warming during 7 hours gradually to 70°. After working up and recrystallisation of the solid product from alcohol *β*-m-*chlorophenyl-β-phenylpropiophenone*, m. p. 71—72°, separated (Found: C, 78·0; H, 5·3; Cl, 11·4. $C_{21}H_{17}OCl$ requires C, 78·6; H, 5·3; Cl, 11·1%). The yield was 1·2 g. from 4 g. of unsaturated ketone, and 3 g. of the latter were recovered.

β-Phenylcrotonophenone (dypnone) and benzene. This reaction occupied 22 hours and two products were separated. The first was recovered from the steam-distillate as a colourless solid, after removal of the excess of solvent. Recrystallisation from alcohol gave *β*-phenylbutyrophenone as colourless leaflets, m. p. 73—74° (Wohler, *Amer. Chem. J.*, 1904, **31**, 655, records m. p. 74°) (Found: C, 85·4; H, 7·2. Calc. for $C_{16}H_{14}O$: C, 85·7; H, 7·2%). The second product was obtained from the ethereal extract of the residue after steam-distillation; recrystallisation of the crude solid from alcohol gave *ββ*-diphenylbutyrophenone as fine needles, m. p. 100—102° (Wohler, *loc. cit.*, gave m. p. 103°), the identity being confirmed by preparation of the oxime, m. p. 162° (Wohler, *loc. cit.*, gave m.p. 163°).

Cinnamylideneacetophenone and benzene. This reaction (which required 6 hours for completion) gave *βδδ-triphenylvalerophenone* which recrystallised from aqueous alcohol (charcoal) in fine needles, m. p. 114—115° (yield, 46%) (Found: C, 88·9; H, 6·5. $C_{29}H_{24}O$ requires C, 89·2; H, 6·7%). Oxidation with alkaline permanganate yielded benzophenone.

The attempted addition of benzene to cinnamylideneacetone (4·8 g.) was unsuccessful. The intermediate was a brownish paste in contrast to the red solid formed by cinnamylideneacetophenone. After 30 hours' stirring the mixture was worked up as usual and a yellow oil (5 g.) was obtained which failed to give any ketone derivative.

β-Naphthylacrylophenone and benzene. A somewhat larger proportion of catalyst (three mols.) was found necessary in order to achieve complete dissolution of the primary addition complex. The reaction was allowed to proceed for 30 hours, and after separation and purification *ββ*-diphenylpropiophenone was obtained in 60% yield, having m. p. and mixed m. p. 91—92°.

Unsuccessful attempts were made to effect reaction between benzylideneacetophenone and iodobenzene, anisole, ethyl benzoate, nitrobenzene, dimethylaniline, naphthalene (in carbon disulphide), and pyridine, and also between *m*-nitrobenzylideneacetophenone and benzene, despite prolonged stirring, the addition of up to four molecular proportions of aluminium chloride, and eventual heating.

Isolation and Composition of Intermediate Molecular Compounds.—The anhydrous aluminium chloride employed in all experiments described heretofore was supplied either by British Drug Houses Ltd., or Imperial Chemical Industries Limited, but the specimen used for the preparation of intermediate molecular compounds was freshly prepared from hydrogen chloride and aluminium foil. After purification by sublimation it was stored in a desiccator and shown by analysis to be pure.

A solution of the unsaturated ketone (0·05 mole) in carbon disulphide was added with rapid stirring to a fine suspension of the aluminium chloride (0·0125 mole) in the same medium. The mixture was stirred for 1 hour, then filtered out of contact with moist air, and the solid intermediate product so obtained washed with dry carbon disulphide.

The intermediates formed by benzylidene- and cinnamylidene-acetophenone could be kept for day without deterioration in a vacuum-desiccator.

Analyses.—(i) A weighed sample of the intermediate in a small glass tube was immersed in an excess of acidified silver nitrate solution contained in a stoppered (ground-glass) flask; this was heated at 100° for 1 hour and the precipitated silver chloride washed with alcohol and ether in turn, dried, and weighed. (ii) The intermediate was hydrolysed as described above, and the chlorine content determined by the Volhard method. (iii) A weighed sample of the intermediate was hydrolysed with dilute acid at 100°, organic matter was removed from the cooled solution, and the aluminium content determined by the " oxine " method.

Inaccuracies should be attributed to factors such as slight lack of homogeneity of the sample and the rapid effect of moisture. The data, however, demonstrate beyond reasonable doubt a 1 : 1 molecular composition in each case. The following results are recorded: Benzylideneacetophenone *intermediate*. Found: Cl, 30·1 (gravimetric), 31·4 (volumetric); Al, 8·3. $C_{15}H_{13}O,AlCl_3$ requires Cl, 30·1; Al, 7·9%. Cinnamylideneacetophenone *intermediate*. Found: Cl, 30·4 (gravimetric); Al, 8·4. $C_{17}H_{14}O,AlCl_3$ requires Cl, 29·0; Al, 7·4%.

Reaction of the Benzylideneacetophenone–Aluminium Chloride Intermediate with Benzene.—(i) A suspension of the intermediate (3 g.) in benzene (80 ml.) was stirred for 7 hours at room temperature and then set aside for several weeks. No change was observed and the original unsaturated ketone was recovered unchanged. (ii) A suspension of the complex (6 g.) and aluminium chloride (3·5 g., 1·5 mols.) in benzene was stirred at room temperature; a homogeneous solution was obtained after 3 hours. The product isolated was ββ-diphenylpropiophenone (4 g.), m. p. and mixed m. p. 91—92°. (iii) Reaction with 0·5 mol. of aluminium chloride did not occur.

Thanks are offered to Imperial Chemical Industries Limited, Pharmaceutical Division, for a gift of the specimen of dypnone. The microanalyses were by Drs. Weiler and Strauss.

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327. *The Effect of Particle Size and Deuterium Substitution on the λ-Point in Ammonium Chloride.*

By D. G. THOMAS and L. A. K. STAVELEY.

The final stages of the λ-points in ammonium chloride, monodeutero-ammonium chloride, and trideuterammonium chloride have been examined dilatometrically with temperature control to $\sim \pm 0{\cdot}002°$. The transitions in the partly deuterated salts, like that in ammonium chloride, reach completion almost isothermally, and hysteresis is associated with the nearly vertical part of the volume–temperature curves. This is in contrast to the transition in tetradeuterammonium chloride which is known to be continuous throughout and free from hysteresis.

The salts examined were prepared by reaction of equimolecular quantities of the component gases. The products were found by electron-microscope examination to consist of very small crystals. The hysteresis loop for these small crystals of ammonium chloride was appreciably narrower than that for larger crystals, but the mean transition temperature was almost unchanged.

A CAREFUL dilatometric investigation by Smits and his co-workers of the λ-point transitions in ammonium chloride and tetradeuterammonium chloride revealed interesting qualitative differences [Smits and MacGillavry, *Z. physikal. Chem.*, 1933, *A*, **166**, 97 (NH_4Cl); Smits, Muller, and Krōger, *ibid.*, 1937, *B*, **38**, 177(ND_4Cl)]. Whereas the transition in the tetradeuter-salt is completely continuous and without hysteresis, that in ammonium chloride is discontinuous (*i.e.*, isothermal) in its closing stages, with a hysteresis loop $\sim 0{\cdot}3°$ wide. The object of the experiments described in this paper was to discover whether there is a gradual change in these characteristics between the extremes of ammonium chloride and tetradeuterammonium chloride, or whether on replacement of hydrogen by deuterium the discontinuity in the transition and the hysteresis disappear before substitution is complete. Ideally, such experiments would be performed on the salts, mono- and tri-deuterammonium chloride, each containing one kind of cation only, *i.e.*, such that every cation in the first salt, for example, would be NH_3D^+. An attempt was made to prepare such samples of mono- and tri-deuterammonium chloride by slow reaction of equimolecular quantities of ammonia and deuterium chloride, and tri-deuterammonia and hydrogen chloride, respectively, in a dry atmosphere at 0°, though without a spectroscopic investigation there is no guarantee that isotopic redistribution did not occur during the preparation.

Crystals of ammonium chloride, prepared in this way from ammonia and hydrogen chloride, were shown by the electron microscope to be extremely small. Since little is known of the effect of crystal size on gradual transitions, it was thought worth while to compare the behaviour of this product with that of much larger crystals obtained from it by sublimation. The same comparison of the small with the sublimed crystals was also carried out with mono- and tri-deuterammonium chloride. Here, sublimation not only increases the crystal size, but almost certainly brings about as well some isotopic redistribution.

EXPERIMENTAL.

For the investigation of hysteresis effects a dilatometric method is undoubtedly the best, since the measurements are made isothermally, and volume changes can be determined with great precision. Each transition was studied in this way over a range of a few degrees. The nature of the problem is such that it demands (*a*) a high degree of temperature control, (*b*) extreme purity of the materials. With the thermostat described below, the temperature was controlled to within $\pm 0{\cdot}002°$.

Dilatometers.—For the investigation of a salt, two similar dilatometers were used, one for the small

crystals, and one for the large ones obtained from them by sublimation. The bulb had a capacity of 7—8 c.c. and held about 3 g. of salt; the calibrated portion of the vertical capillary in which volume changes were observed had a length of 36 cm. and a cross section of 0·002 sq. cm. In a preliminary investigation of the small crystals in ammonium chloride a modified dilatometer was used in which the graduated capillary was in a horizontal position and mercury was used as the confining fluid. The magnitude of the volume change accompanying the transition as found with this apparatus was appreciably greater than that recorded by Smits *et al.* (*loc. cit.*); furthermore, it was observed that when the pressure on the mercury surface was increased by about an atmosphere there was an apparent volume change in the dilatometer of the order of 1 c.c. That this was not due to gas in the dilatometer (an extremely unlikely contingency in view of the thorough evacuation of the salt before admission of mercury), was shown by the fact that the volume changes consequent upon the progressive increase in pressure did not conform to those predicted by the gas laws. Electron-microscope photographs (see below) showed that the crystals were extremely small, and these curious volume changes were ascribed to the effect of pressure in forcing the mercury, which presumably does not wet ammonium chloride, into the many minute crevices that must have been present between such small crystals. This appears to be a serious drawback to the use of mercury as a dilatometric fluid when examining small particles; otherwise it has much to recommend it (Bekkedahl, *J. Res. Nat. Bur. Stand.*, 1949, **43**, 145). It was accordingly decided to use carbon disulphide as the confining fluid, and in order to examine the effect, if any, of crystal size on the nature of the transition, samples of large and small crystals were compared simultaneously in two dilatometers, the large crystals being made from the small by sublimation.

The dilatometers were filled with salt through a tube joined on to the bulb which was subsequently sealed off, the weight of salt being obtained by difference. This operation involved exposure of the salts to the atmosphere for a short time. The dilatometers were then sealed on to the vacuum system, and thoroughly evacuated through both the capillary tube and a wider tube joined directly to the bulb which was later sealed off. Carbon disulphide, purified by shaking with mercury and fractionation, was poured into a trap system, with mercury cut-offs (Shapiro, *Analyt. Chem.*, 1949, **21**, 888) in place of greased taps, dried with phosphoric oxide, and carefully degassed, after which it was distilled into the evacuated dilatometers.

After adjustment of the amount of fluid so that the transition occurred when the meniscus was near the centre of the capillary, the tops of the dilatometers were sealed off.

Variations due to changes in the room temperature of the volume of carbon disulphide which was not in the thermostat, were approximately corrected for by observing the variations in a " dummy " capillary similar to those of the dilatometers, but terminating just above the thermostat fluid.

The work of Smits *et al.* (*loc. cit.*) and others has indicated that the hysteresis effects cannot be eliminated or materially altered by waiting for periods of time of the order of a day. We have accepted this and have carried out no further investigations of the point. Above or below the nearly vertical limbs of the hysteresis loops the volume became constant almost at once; on the limbs themselves the volumes became virtually constant after one or two hours.

Thermostat, Temperature Control, and Measurement.—The thermostat used was similar to that described by Scott and Brickwedde (*J. Res. Nat. Bur. Stand.*, 1931, **6**, 401), except that the heating current was controlled by a vapour-pressure regulator which was filled with methyl chloride. Solid carbon dioxide was used as the refrigerant.

Methyl chloride was obtained from a cylinder and purified by distillation in a low-temperature column (Clusius and Riccoboni, *Z. physikal. Chem.*, 1938, *B*, **38**, 81). A small bulb in the thermostat contained about ½ c.c. of liquid methyl chloride, and the pressure of its vapour supported a column of mercury; the meniscus on the evacuated side of this column could make contact with a pointed wire and open and close a circuit operating a relay which controlled the heating current. Such a regulator, having a small heat capacity, responds very rapidly to changes of temperature. Methyl chloride was chosen because it has a suitable vapour pressure (½—1½ atm.) over the temperature range under investigation. The mercury column was surrounded by a jacket through which water from a thermostat was pumped. The temperature at which the regulator operated was changed by altering the quantity of mercury in it by means of a mercury reservoir and a system of taps; fine adjustment was obtained by running mercury into or out of a capillary tube.

The temperature of the thermostat was measured with a methyl chloride vapour-pressure thermometer. The pressures were read to ±0·01 mm. on a steel scale which had been compared with a Geneva glass scale. The corresponding temperatures were calculated from Messerly and Aston's data (*J. Amer. Chem. Soc.*, 1940, **62**, 886). The absolute accuracy of the temperature measurements was checked with a platinum resistance thermometer: at an arbitrary temperature it read −30·67°, while the vapour-pressure thermometer gave −30·67$_2$°.

Preparation of Materials.—Ammonia. Synthetic ammonia was passed through a dust trap and over potassium hydroxide pellets. For final drying it was condensed over clean sodium and kept in contact with it as a liquid overnight; it was then submitted twice to fractional sublimation, and finally the middle fraction was stored in a globe.

Trideuterammonia was prepared by reaction of 99·7% deuterium oxide with magnesium nitride. The nitride was made by passing cylinder nitrogen over hot copper, through a liquid-air trap, and then over magnesium at red heat; immediately before the reaction with deuterium oxide vapour it was degassed *in situ* at 400°. The crude trideuterammonia contained much deuterium oxide, and was therefore passed back and forth several times over the nitride, which was heated in the final stages. After being kept in contact with more nitride, and then dried with sodium, the trideuteroammonia was finally purified in the low-temperature fractionating column from a bath of boiling " Freon."

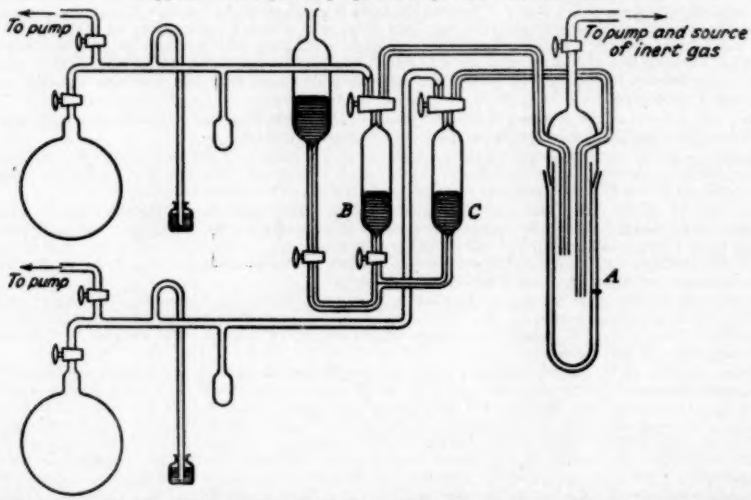
Hydrogen and deuterium chlorides. These were prepared respectively from water and 99·7% deuterium oxide, by the method described by Brown and Groot (*J. Amer. Chem. Soc.*, 1942, **64**, 2223). Both gases were finally purified by fractionation at −78°.

Preparation of salts. The salts were prepared from the component gases in the apparatus shown in Fig. 1: *B* and *C* are two similar vessels, 20 cm. long and of 2·8 cm. internal diameter, one of which contained ammonia or trideuterammonia at a pressure a little below atmospheric, the other hydrogen chloride or deuterium chloride at an equal pressure. By admitting mercury into these vessels simultaneously the two gases were slowly forced into the reaction chamber *A*, which contained nitrogen at approximately the same pressure as that of the reacting gases. These were led into *A* by capillary tubes, that conducting the lighter gas terminating below the other. All the salt collected in the inner tube in *A*, which was 27 cm. long and 2·5 cm. in diameter, and by disconnection of the cone and socket, the salt could easily be transferred to another vessel. *A* was surrounded by ice, to minimise any local heating of the gases or product and hence to reduce the chance of isotopic redistribution. Each charge was introduced during 10—15 minutes. Usually about 20 charges could be admitted before the apparatus became blocked; the reaction of the gases did not seem to be complete, probably partly owing to diffusion effects and partly to the fact that exactly equivalent proportions of the reactants were not used, as the pressure in *A* slowly increased. The salt was finally thoroughly evacuated to remove any unreacted gases.

The salt so formed consisted of a powder made up of minute crystals (see below). In order to obtain larger crystals, about half of the product (~3 g.) was sublimed, by placing it at the bottom of a tube 2·8 cm. in diameter, filling this with dry nitrogen at 0·5 cm. pressure, and immersing the lower portion of the tube in an oil-bath at 250°. The salt sublimed to form a hard crust on the glass just above the liquid level; it was scraped off and finally crushed in a mortar. The crystals were perhaps 0·1 mm. long.

FIG. 1.

Apparatus used for the preparation of ammonium chlorides.



Experimental Results.—The powders made by mixing the gases were examined with an electron microscope. We are much indebted to Dr. K. Little and to the Diffraction Group at the Atomic Energy Research Establishment, Harwell, for taking these photographs for us. The ammonium chloride was found to consist of crystals beyond the limit of resolution of the instrument. Shadowing with gold vapour revealed particles with linear dimensions between 120 and 20 A.; it would not be possible to detect particles smaller than 20 A. The monodeuterammonium chloride consisted mostly of similar particles though some appeared to be cubes with sides between 200 and 1000 A., and occasionally as large as 4000 A. Unfortunately, it was not possible to disperse the trideuterio-compound, and poor photographs were obtained; but again it appeared that the particles were very small.

It is possible that crystals larger by several powers of ten were present, but were not included in the sample examined by the electron microscope; however, this seems unlikely, as the conditions of formation were kept as uniform as possible.

The results of the dilatometric investigations are presented as molar volumes at different temperatures. The relative accuracy of the molar volumes is of course much higher than the absolute accuracy.

Briefly, the molar volumes were calculated as follows. The mass of salt is known; from the volume changes just above the transition, the coefficient of expansion of all the salts being assumed to be the same as that found by Simon and Bergmann for ammonium chloride at this temperature (*Z. physikal. Chem.*, 1930, *B*, **8**, 255), the quantity of fluid in the dilatometer may be approximately calculated. Hence it is possible to assess the volume changes due to the salt itself. An approximate value of the molar volume at a particular point was taken to be absolutely correct and so the molar volumes at the remaining points were calculated.

Figs. 2—7 show the plots of *V*, the molar volume, against *T*, the temperature, for the large and small crystals of the three salts examined. Selected points from the graphs are given in Table I.

FIG. 2.
NH_4Cl, *small crystals.*

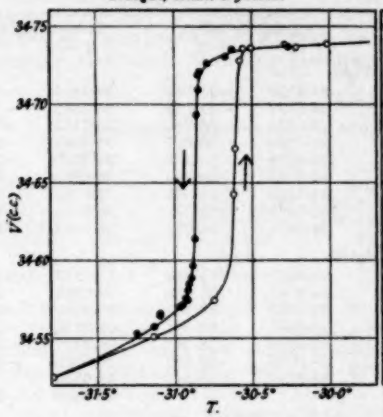


FIG. 3.
NH_4Cl, *sublimed crystals.*

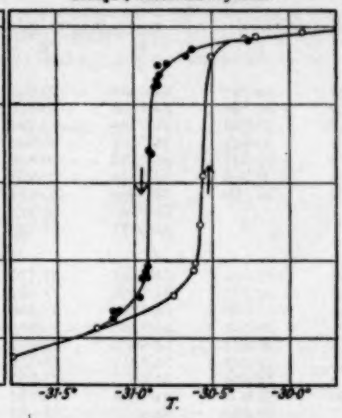


FIG. 4.
NH_3DCl, *small crystals.*

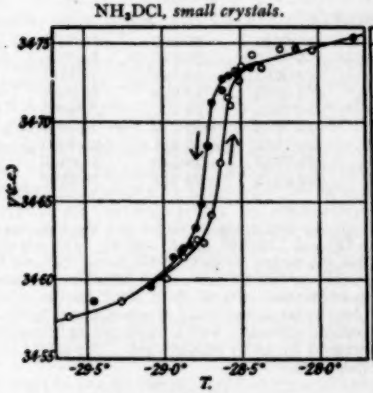


FIG. 5.
NH_3DCl, *sublimed crystals.*

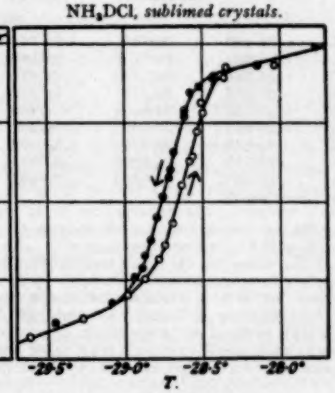


FIG. 6.
ND_3HCl, *small crystals.*

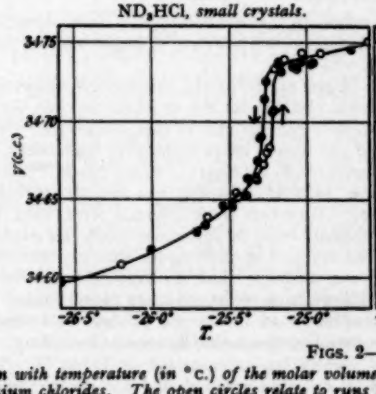
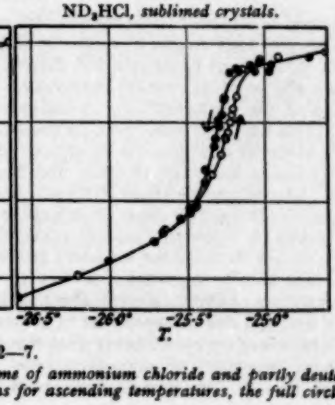


FIG. 7.
ND_3HCl, *sublimed crystals.*



FIGS. 2—7.

Variation with temperature (in °C.) of the molar volume of ammonium chloride and partly deuterated ammonium chlorides. The open circles relate to runs for ascending temperatures, the full circles to those for descending temperatures.

TABLE I.

Small crystals.				Large crystals.			
Ascending temp.		Descending temp.		Ascending temp.		Descending temp.	
V.	*T.*	*V.*	*T.*	*V.*	*T.*	*V.*	*T.*
			NH_4Cl.				
34·5251	−31·781°	34·7406	−29·615°	34·5379	−31·781°	34·7414	−30·262°
34·5510	−31·138	34·7353	−30·628	34·5623	−31·138	34·7262	−30·788
34·5740	−30·745	34·7264	−30·788	34·5774	−30·745	34·7113	−30·867
34·6429	−30·617	34·7191	−30·842	34·5940	−30·617	34·7037	−30·880
34·6718	−30·607	34·7092	−30·846	34·6230	−30·575	34·6705	−30·903
34·7283	−30·575	34·6164	−30·867	34·6543	−30·556	34·6683	−30·890
34·7367	−30·219	34·5968	−30·880	34·7309	−30·505	34·5966	−30·912
		34·5760	−30·925	34·7429	−30·289	34·5764	−30·962
		34·5571	−31·133	34·7465	−30·018	34·5568	−31·241
			NH_3DCl.				
34·5764	−29·618	34·7537	−27·777	34·5632	−29·618	34·7477	−27·777
34·5861	−29·277	34·7306	−28·521	34·5901	−28·984	34·7283	−28·432
34·6238	−28·742	34·7273	−28·616	34·6132	−28·783	34·7190	−28·576
34·6412	−28·691	34·7126	−28·684	34·6365	−28·691	34·7040	−28·611
34·6745	−28·632	34·6855	−28·704	34·6788	−28·561	34·6702	−28·704
34·7105	−28·561	34·6852	−28·717	34·7062	−28·497	34·6535	−28·754
34·7159	−28·580	34·6488	−28·754	34·7350	−28·248	34·6155	−28·873
34·7260	−28·506	34·6332	−28·792			34·5860	−29·089
34·7457	−28·039	34·6227	−28·832				
		34·5955	−29·089				
			ND_3HCl.				
34·6083	−26·203	34·7451	−24·713	34·6014	−26·203	34·7418	−24·713
34·6380	−25·645	34·7319	−25·165	34·6313	−25·645	34·7340	−25·187
34·6729	−25·284	34·7253	−25·261	34·6661	−25·348	34·7153	−25·261
34·6806	−25·255	34·7147	−25·279	34·6790	−25·284	34·7048	−25·279
34·6804	−25·259	34·6903	−25·299	34·6933	−25·241	34·6972	−25·299
34·6938	−25·241	34·6898	−25·301	34·7048	−25·219	34·6843	−25·326
34·7062	−25·223	34·6750	−25·320	34·7162	−25·181	34·6695	−25·385
34·7079	−25·219	34·6639	−25·385	34·7338	−25·143	34·6455	−25·486
34·7376	−25·181	34·6456	−25·483	34·7413	−24·911	34·6109	−26·010
34·7504	−24·609						

Our results for ammonium chloride may be compared with those of Smits and MacGillavry (*loc. cit.*). For the limits of the hysteresis loop they give −30·79° and −30·52°, mean −30·65°, which is about 0·07° higher than our value for the mean temperature for the larger crystals. We do not believe our values for the absolute temperatures to be in error by as much as this in view of the satisfactory check already noted carried out with a platinum-resistance thermometer. Smits gives 0·27° as the width of the hysteresis loop, whereas we found 0·35° and 0·25° for the large and small crystals, respectively. It may be that Smits's method of preparation of ammonium chloride, which involved sublimation at low temperatures, gave smaller crystals than those obtained by us by sublimation; this might account for the difference between his and our values for the loop width.

DISCUSSION.

It is hoped to consider these results with others of the same kind in a later paper, in which the possibility of formulating a comprehensive theory of hysteresis in phase transitions will be examined; the present discussion will therefore be brief.

Perhaps the most interesting observation in our study of the ammonium chlorides is the contraction of the hysteresis loop in ammonium chloride as the crystals become very small. Hitherto, there has been little work on the effect of particle size in this connection. Attempts have been made to vary the size of crystals of condensed gases displaying transitions, but the hysteresis remains unaltered (Eucken and Bartholomé, *Göttingen Nachr.*, Math.-Phys. Kl. II, 1936, **2**, 53; Clusius and Weigand, *Z. Elektrochem.*, 1938, **44**, 679), but it is doubtful if really small crystals can be obtained in these circumstances. Dinichert (*Helv. Physica Acta*, 1944, **17**, 400), however, found by dielectric-constant measurements that, in agreement with our experiments, the hysteresis loop is narrower for finely ground crystals of ammonium chloride than for single crystals. But he also reported, contrary to our findings, that the transition in the smaller crystals was more diffuse. Nevertheless, it follows from what we have found that if in ideal crystals of uniform size the final part of a transition is an isothermal process, in a sample consisting of crystals of widely differing sizes the closing stages would appear to be diffuse.

The more important of our quantitative results are summarised in Table II. Those so Smits *et al.* (*loc. cit.*) on tetradeuterammonium chloride are included for comparison; T_w if

the temperature at which, on warming, dV/dT is a maximum, and T_c the corresponding temperature on cooling; T_m is the mean of T_w and T_c. ΔT is the width of the hysteresis loop approximately half-way up the almost vertical part of the curves. ΔV is that part of the molar-volume change which occurs comparatively abruptly, though it is difficult to assess this with any accuracy, particularly for the sublimed samples of the partly deuterated salts.

TABLE II.

Summary of the transition characteristics in ammonium chlorides.

	NH_4Cl.		NH_3DCl.		ND_3HCl.		ND_4Cl
	Small.	Large.	Small.	Large.	Small.	Large.	
T_w	−30·61°	−30·55°	−28·61°±0·03°	−28·55°±0·05°	−25·22°±0·03°	−25·21°±0·04°	−23·4°
T_c	−30·86°	−30·90°	−28·72°±0·03°	−28·68°±0·05°	−25·27°±0·01°	−25·28°±0·05°	−23·4°
T_m	−30·735°	−30·725°	−28·665°	−28·62°	−25·245°	−25·245°	−23·4°
ΔT	0·25°	0·35°	0·10°	0·12°	0·06°	0·07°	0°
ΔV	0·15	0·15	0·10	0·11	0·06	0·07	0

The transition temperature (as assessed by T_w, T_c, or T_m) varies almost, but not exactly, linearly with deuterium content. Thus, T_m for the large crystals of mono- and tri-deuter-ammonium chloride, calculated on the assumption of a linear variation from ammonium to tetradeuterammonium chloride, would be −28·895° and −25·23°, as compared with the experimental figures of −28·62° and −25·245°. The discrepancy for the monodeuterio-salt is small, but we consider real. Linear variation of transition temperature with deuterium content in mixed crystals of isotopic molecules has been found for the systems HBr–DBr (Clusius, *Z. Naturforsch.*, 1946, **1**, 142) and CH_4–CD_4 (Bartholomé, Drikos, and Eucken, *Z. physikal. Chem.*, 1938, *B*, **39**, 371).

The experiments with ammonium chloride show that the change in crystal size brought about by sublimation does not in itself make the final volume change any less abrupt. However, on sublimation of the partly deuterated salts, the closing stages of the transitions certainly become more diffuse; this can therefore be ascribed to some isotopic redistribution occurring during sublimation, so that the salt virtually becomes a mixed crystal of the five possible ammonium chlorides. The comparative sharpness of the completion of the transitions in the original samples suggests that the cations in any one of these are mainly of one kind. Nevertheless, the mean temperatures of the transitions in mono- and tri-deuterammonium chloride are scarcely altered by sublimation. This is in harmony with the observation that the transition temperature of mixed crystals of 75% of methane and 25% of tetradeuteriomethane is the same as that of pure monodeuteriomethane (Bartholomé, Drikos, and Eucken, *loc. cit.*).

The figures in Table II show that there is a rough correspondence between the widths of the hysteresis loops and the magnitudes of the comparatively abrupt volumes changes. It seems that these quantities are altered most by the initial introduction of deuterium into ammonium chloride or of hydrogen into tetradeuterammonium chloride.

Although in the transitions we have examined part of the volume change occurs within a very small temperature range, it is not true to say that a discontinuous volume change occurs at any particular temperature. Impurities, however, undoubtedly tend to make sharp transitions diffuse [cf. the observations on ammonium bromide (Smits, Ketelaar, and Muller, *Z. physikal. Chem.*, 1936, *A*, **175**, 359) and the effect of isotopic redistributions commented on above]; strains in crystals may have the same effect, and our own observations show that the transition temperature is a function of crystal size. These factors will combine to make somewhat diffuse a volume change which would occur discontinuously in pure, unstrained crystals of uniform size. We therefore agree with Smits's conclusion that ideally the final part of the transition in ammonium chloride occurs isothermally, and we consider that this is also true for mono- and tri-deuter-ammonium chloride. It therefore appears from the experiments on "light" and "heavy" ammonium chloride, bromide, and iodide that, as Smits has implied, hysteresis only occurs when part of the transition is sharp, but that hysteresis is absent when the transition is completely continuous. We hope in a later paper to consider whether or not this generalization can be applied to transitions in other substances.

We thank Prof. K. Clusius for a gift of heavy water, and Dr. B. Lambert for constructing some of the glass apparatus.

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328. *The Kinetics of the Photolysis of Acetaldehyde. Part I. The Determination of Ethane and Hydrogen in the Reaction Products by the Use of a Mass Spectrometer.*

By C. J. Danby, A. S. Buchanan, and I. H. S. Henderson.

Ethane and hydrogen have been determined in the products of the high-temperature (300°) photolysis of acetaldehyde by the use of a mass spectrometer. The influence of acetaldehyde pressure and of temperature on their formation has been studied.

The photolysis of acetaldehyde by ultra-violet light at about 300° takes place by a chain process of considerable chain length. It is probable that methyl radicals are the chain-propagating particles and that chain-termination occurs by the recombination of two methyl radicals to form ethane according to the scheme:

$$CH_3{\cdot}CHO + h\nu = CH_4 + CO \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$CH_3{\cdot}CHO + h\nu = CH_3{\cdot} + {\cdot}CHO \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

$$CH_3{\cdot} + CH_3{\cdot}CHO = CH_3{\cdot} + CH_4 + CO \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

$$CH_3{\cdot} + CH_3{\cdot} = C_2H_6 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

(cf. Leermakers, *J. Amer. Chem. Soc.*, 1934, **56**, 1537; Akeroyd and Norrish, *J.*, 1936, 890).

This mechanism does not take into account any subsequent reaction of the formyl radicals produced in reaction (2). Haden and Rice (*J. Chem. Physics*, 1942, **10**, 445) have suggested the following chain reaction:

$${\cdot}CHO + CH_3{\cdot}CHO = CH_4 + CO + {\cdot}CHO \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

$$CH_3{\cdot} + {\cdot}CHO = CH_3{\cdot}CHO \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

This requires that the formyl radical should be fairly stable at high temperatures.

An alternative process is:

$${\cdot}CHO = H + CO \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

$$H + CH_3{\cdot}CHO = CH_4 + CO + H \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

$$H + CH_3{\cdot}CHO = CH_3{\cdot} + CO + H_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

$$H + H + (M) = H_2 + (M) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (10)$$

Experiments on the photolysis of methyl iodide (West and Schlesinger, *J. Amer. Chem. Soc.*, 1938, **60**, 961), dimethylmercury (Gomer, *J. Chem. Physics*, 1950, **18**, 998), and acetone (Trotman-Dickenson and Steacie, *ibid.*, p. 1097) have shown that the bimolecular association of two methyl radicals to form ethane occurs readily.

The participation of reaction (4) and of reactions (7)—(10) in the high-temperature photolysis of acetaldehyde can only be established by analysis of the reaction products for ethane and hydrogen. From the known chain length of the reaction, however, the concentrations of ethane and hydrogen to be expected are about 1% of the reaction products. The unambiguous detection of concentrations of this order is hardly practicable by normal methods of gas analysis.

By the use of a mass spectrometer it has now been found possible not only to detect ethane and hydrogen in the products of the photolysis of acetaldehyde at temperatures between 212° and 340° but also to measure the changes in concentration produced by changes in initial aldehyde pressure and temperature.

The Principles of Gas Analysis by the Use of the Mass Spectrometer.—Although the general principle of the mass spectrometer is familiar the practical application of the instrument to the analysis of mixtures of organic compounds is perhaps neither obvious nor well known and a short summary will be given here. Organic molecules are dissociated when bombarded by electrons of adequate energy to form a variety of positive ions. In a mass spectrometer these ions are resolved according to their ratio of charge to mass, and their relative abundances

determined as deflections of an indicating or recording instrument. In general, the mass spectrum of an organic molecule is fairly complex. In addition to the positive ion corresponding to the undissociated molecule there will also be ions due to fragments produced by the dissociation of the molecule in almost all possible ways. Doubly charged ions may also be present. The relative abundances of these different ions may differ by several powers of ten.

The use of the mass spectrometer for the analysis of mixtures of organic compounds depends on the fact that under carefully controlled conditions the *relative abundance* of the different ions produced by a given molecule remains constant. This pattern may therefore be used to identify the molecule. At the same time the *absolute abundance* of the ions is proportional to the partial pressure of the substance in the ionisation chamber of the instrument. Both the mass spectrum and the relation between ion abundance and partial pressure (the " sensitivity ") have to be determined empirically for each possible component of a mixture by separate experiments with pure samples.

The mass spectrum of a mixture is the sum of the spectra of the constituents, each multiplied by the sensitivity for that constituent and by its partial pressure. These mass spectra will inevitably overlap, *i.e.*, ions of the same mass will appear in the spectra of many of the components. The observed abundance at many mass numbers in the spectrum of the mixture will hence be the sum of contributions from a number of constituents.

There are several ways in which the composition of the mixture may be calculated from the data of the mass spectrometer. In general, we obtained a set of linear simultaneous equations of the form :

$$a_p k_a + b_p k_b + c_p k_c + \ldots = m_p$$
$$a_q k_a + b_q k_b + c_q k_c + \ldots = m_q$$
$$a_r k_a + b_r k_b + c_r k_c + \ldots = m_r$$
etc.

where a_p, a_q, a_r, . . . are the ion abundances at mass numbers p, q, r, ... given by unit partial pressure of substance A; b_p, b_q, b_r, . . . and c_p, c_q, c_r, . . . being the corresponding data for for substances B and C. The ion abundances at the same mass numbers given by unit amount of the mixture are m_p, m_q, m_r, ... This set of equations must be solved for the coefficients k_a, k_b, k_c, . . . which are the proportions of A, B, C . . . in the mixture.

With relatively simple mixtures it is sometimes possible to find a mass number in the mixture spectrum which appears in the mass spectrum of only only of the constituents. This greatly simplifies the calculation as the abundance of this ion can be related immediately to the partial pressure of the substance producing it by means of the data of the calibration experiments. This was possible in the present work.

Experimental.

The acetaldehyde was photolysed in a silica vessel of about 100 ml., having plane windows and kept at the required temperature in a temperature-controlled furnace. It was connected to storage vessels for reagents, manometer, Töpler device for removing samples of the reaction product, and the usual system of pumps. The light source was a 500-w. mercury lamp radiating principally at 3600 A., the output being kept constant by manual control of the current. Acetaldehyde was purified by neutralisation of free acid followed by distillation and storage under nitrogen. Before use it was redistilled *in vacuo*.

Samples of reaction products were passed repeatedly through moist sodium hydrogen sulphite on pumice (which reduced the aldehyde concentration to a value undetectable by the mass spectrometer), dried by solid potassium hydroxide, and transferred to the mass spectrometer in small vessels fitted with a tap and standard ground joint.

A Metropolitan-Vickers mass spectrometer Type M.S.2 was used. This is a Nier-type instrument fitted with a pen recorder. In all experiments an ionising electron energy of 70 ev. was used. The gas samples were measured in terms of pressure in a constant-volume gas pipette of about 3-ml. volume and were then allowed to expand into a 5-l. vessel communicating with the ionisation chamber through a small leak. The temperatures of the gas pipette and the reservoir were measured and corrections applied to allow for any changes.

The pressure of gas in the ionisation chamber is proportional to the rate of flow through the leak and hence to the pressure in the reservoir (the pressure in the ionisation chamber being negligible compared with this). The pressure in the reservoir is determined by the amount of gas admitted to it, hence the pressure of the gas sample in the gas pipette may be taken as a measure of the pressure in the ionisation chamber.

The amount of gas taken for an analysis is less than 0·5 ml. at N.T.P. and of this only about 1% is actually consumed.

Analytical procedure.

Although the mass spectrum of a molecule and the sensitivity are, in principle, constant under controlled conditions, these conditions are not yet attainable in practice. In spite of precautions there are still uncontrolled and largely unknown variables which can cause changes in mass spectra. These phenomena are not faults in the particular instrument used but arise to a greater or lesser extent with all mass spectrometers at the present time. Changes in the *relative* ion abundances given by a substance are usually small and errors from this cause may be practically eliminated by carrying out frequent calibration experiments. More serious are changes in sensitivity which are often large. These changes can be detected and corrections applied by the use of an internal standard reference gas. In the present work neon has been used for this purpose. None of the substances present in the acetaldehyde photolysis products gives rise to ions of masses 20 or 22. Ions at these mass numbers were therefore unambiguously due to neon. A measured partial pressure of pure neon was added to all gas samples and the recorded neon ion abundances compared with a standard value. The actual sensitivity of the instrument during the tracing of each mass spectrum was thus determined, and the appropriate corrections could be applied to the measured abundances to bring them all to a standard level of sensitivity.

The reaction products of the photolysis consist largely of carbon monoxide and methane, the unchanged acetaldehyde having been removed chemically. The relative abundances of the more important positive ions in the mass spectra of the possible constituents are given in Table I.

Table I.

Mass spectra of possible constituents of the reaction products.

Relative positive ion abundances.

Mass no.	$CH_3{\cdot}CHO$.	C_2H_6.	CH_4.	CO.	Mass no.	$CH_3{\cdot}CHO$.	C_2H_6.	CH_4.	CO.
12	1·5	0·6	1·3	1·2	27	5·9	108·6	—	—
13	6·9	1·5	4·1	—	28	7·1	360·0	—	100·0
14	20·2	7·0	9·5	—	29	156·0	83·5	—	1·2 ($^{13}C^{16}O$)
15	59·3	9·7	79·5	—	30	1·8	100·0	—	0·2 ($^{12}C^{18}O$)
16	8·6	—	100·0	0·3	42	16·1	—	—	—
25	5·1	11·0	—	—	43	57·3	—	—	—
26	10·5	72·5	—	—	44	100·0	—	—	—

In this table the ions corresponding to the undissociated molecules have been taken as having an abundance of 100·0. Only the more abundant ions have been included.

From this Table it is evident that it is not practicable to use the abundance of the $C_2H_4^+$ ion to determine small amounts of ethane in the reaction products because carbon monoxide, which is present in very large amount, gives an ion of the same mass (CO^+). The same is true to a lesser extent with masses 29 and 30 where there are contributions from carbon monoxide ions containing the heavy isotopes of carbon and oxygen. Ethane was therefore determined from the abundance of the ion of mass 27 which appears in the ethane spectrum only. The contribution of ethane at mass 15 was then calculated and subtracted from the observed abundance at this mass, leaving the contribution due to methane, from which the methane pressure was calculated.

Hydrogen was estimated from the mass 2 ion abundance. With the positive ion beam focussing potentials set at the optimum values for ions of masses between 12 and 50 the sensitivity of the instrument at mass 2 is small. The precision of the estimation of hydrogen is therefore considerably less than that for ethane.

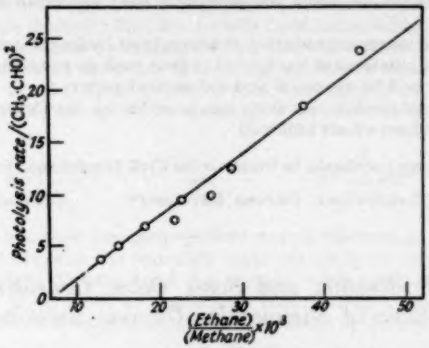
Results.

Table II gives the analytical results for a series of reaction product samples obtained by varying the initial aldehyde pressure at a constant temperature (300°). Table III gives the corresponding results for the photolysis of the same initial pressure of aldehyde at different temperatures.

Duplicate analyses were made on two of the reaction product samples after a lapse of several days during which the ion source of the mass spectrometer was dismantled and a new filament fitted. These analyses (which are shown in Table II) show that the estimation of ethane when present to the extent of 0·5—1% is reproducible to about 1·5% of this value.

Blacet (*J. Phys. Chem.*, 1948, **52**, 540), using a mass spectrometer, was unable to detect ethane in the products of the low-temperature acetaldehyde photolysis. The results in

Table II show that the proportion of ethane is increasing with decreasing temperature down to about 200°. It would appear that either a different mechanism of reaction is predominant at



lower temperatures, or that the previous analytical work was not sufficiently sensitive to detect the ethane.

TABLE II.

Experiments with variable aldehyde pressure at 300°.

Initial CH_3·CHO pressure, mm.	Initial photolysis rate.	Ethane in total product, moles %.	Moles (%) in product free from CH_3·CHO. Ethane.	Hydrogen.	Ratio, $\frac{[C_2H_6]}{[CH_4]} \times 10^3$.
19·4	0·90	1·05	2·15	2·58	4·45
30·8	1·75	0·96	1·83	—	3·76
61·6	4·62	0·82	1·40	—	2·86
80·0	6·45	0·79	1·28	—	2·62
112·0	9·20	0·67	1·07	—	2·18
161·2	17·8	0·62, 0·63	0·90, 0·91	1·05	1·82
224·0	25·0	0·51	0·74	—	1·50
317·3	38·8	0·50, 0·51	0·60, 0·61	0·70	1·29

TABLE III.

Experiments with constant aldehyde pressure at different temperatures.

Initial CH_3·CHO pressure, mm.	Temp.	Ethane in total product, moles %.	Moles (%) in product free from CH_3·CHO. Ethane.	Hydrogen.
81·1	212°	0·65	2·32	—
81·3	250	0·86	1·97	—
82·5	250	0·74	1·63	1·81
83·0	280	0·76	1·42	—
82·0	300	0·70	1·11	—
80·0	320	0·71	1·07	—
80·0	340	0·68	0·93	—

If we neglect the aldehyde decomposed in the primary process compared with that reacting by the chain propagation reaction we may write :

$$d[CH_3\cdot CHO]/dt = \rho = k_3[CH_3][CH_3\cdot CHO]$$

$$[CH_3] = \rho/k_3[CH_3\cdot CHO]$$

$$d[C_2H_6]/dt = k_4[CH_3]^2 = k_4\rho^2/k_3^2[CH_3\cdot CHO]$$

$$d[CH_4]/dt = \rho$$

Hence

$$\frac{d[C_2H_6]/dt}{d[CH_4]/dt} = \frac{k_4\,\rho}{k_3^2[CH_3\cdot CHO]^2}$$

Or, for an early stage of the reaction :

$$[C_2H_6]/[CH_4] \propto \rho/[CH_3\cdot CHO]^2$$

The figure shows that this relation is approximately obeyed by the analytical results in Table II. Better agreement would not be expected as the relation only applies strictly to initial rates and concentrations while the analytical data are mean values over appreciable time intervals.

The presence, in the reaction products, of amounts of hydrogen comparable with those of the ethane suggests that reactions of the formyl radical such as reactions (7)—(10) may play an appreciable part. This will be discussed in a subsequent paper.

The mass spectrometer used in this work was provided by the Department of Scientific and Industrial Research to whom we are indebted.

We should like to express our thanks to Professor Sir Cyril Hinshelwood for his help and interest.

PHYSICAL CHEMISTRY LABORATORY, OXFORD UNIVERSITY. [*Received, January 17th*, 1951.]

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329. *Orbital Hybridisation and Some Other Considerations concerning the Transition State of Bimolecular Organic Substitution Reactions.*

By V. GOLD.

The plausible orbital hybridisations in the transition state of bimolecular organic substitution reactions can be divided into two classes: (i) those in which a *p*-electron contributes to the binding of three atomic centres, and (ii) those in which only two-centre binding by electron pairs need be postulated. The first category is approximated by the case of substitution at a saturated carbon atom, and the second one by that of aromatic substitution. Substitution at the carbon atom of vinyl or carbonyl groups probably involves an intermediate structure about which it should in principle be possible in some cases to adduce more exact information by stereochemical experiments.

IN this paper the quantum-mechanical picture of the directional properties of single and multiple carbon bonds is applied to a discussion of the connection between electronic arrangement and bond directions in the transition state of bimolecular substitution reactions at a carbon atom and hence the stereochemical course of such reactions. This approach has been indicated by other workers, notably Hughes, Ingold, and their collaborators (*e.g.*, *J.*, 1937, 1256; 1941, 608), for the cases of substitution at a saturated carbon atom or in a benzene ring, but has not so far received a more comprehensive development.

The common feature of all bimolecular substitution reactions—homolytic, nucleophilic, or electrophilic—is the condition that in the transition state the substitution centre must be linked to one atomic nucleus more than in the initial and the final state of the reaction. The combination of this obvious requirement with the postulates that the reactions are electronically "adiabatic" and that the potential energy of the transition state is to be a minimum, forms the basis of the following discussion. It is found that the accepted principles of bonding and hybridisation are adequate for at least a qualitative discussion. For the present no attempt has been made to assess the energy changes involved in the formation of the transition states and thus to decide between possible alternative structures of the transition state.

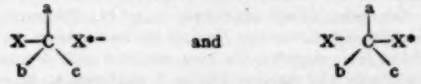
Substitution at a Saturated Carbon Atom.—It is found that bimolecular substitution invariably leads to optical inversion of configuration whenever such a test is possible (Hughes, *Trans. Faraday Soc.*, 1938, **34**, 202). In the transition state of the reaction

$$X{\cdot}C\overset{a}{\underset{b}{\overset{|}{\underset{|}{}}}}c + X^{\bullet} \longrightarrow a\,b\,c\overset{\vdots}{C}{\cdot}X^{\bullet} + X$$

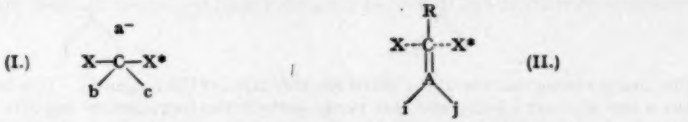
(all electric-charge signs of the species involved being omitted), the groups X and X• must therefore lie on opposite sides of the surface containing the points C, a, b, c. It is usually accepted that the points X, C, and X• will, in the absence of unsymmetrical steric hindrance, be collinear, and that, apart from a slight deviation caused by the possibility of a potential hollow near the saddle point (Gorin, Kauzmann, Walter, and Eyring, *J. Chem. Physics*, 1939, **7**, 633), X and X• will be equidistant from C and hence C, a, b, and c will tend to be coplanar. The hybridisation must then be such that three equal coplanar bonds (to a, b, c) and two, possibly weaker, equal bonds in the direction perpendicular to the plane of this set of three bonds can be formed. The only hybridisation of *s*- and *p*-electrons which can lead to three strong coplanar

bonds is the sp^3 arrangement as assumed for the σ-bonds in ethylene, and we may conclude that the electron contributed towards the binding of the nuclei X and X* is the remaining *p*-electron. As far as this argument goes the problem is the same irrespective of the electric charges of the reaction partners, although this will affect the electron distribution within the bond formed.

In terms of valency-bond representations—which may sometimes be found preferable for the statement of these structures, since they take explicit account of the restrictions on electronic configurations imposed by the Pauli principle—the transition state, for the example of nucleophilic substitution, may be said to be made up of the mesomeric structures



The question arises (as has been privately pointed out to the author by Professor Coulson) whether the weakness of bonds in the transition state can really be thought to be localised in the bonds C–X and C–X*. Valency-bond terminology being used, this raises the problem whether structures such as (I) make an appreciable contribution to the mesomeric transition state. (The hybridisation of the collinear X–C–X bonds would be *sp*, leaving two pure *p*-orbitals



for the bonding of b and c.) Such structures would certainly be unimportant in the case of nucleophilic replacements such as the hydrolysis of alkyl halides and, in any case, it seems reasonable in the first approximation to assume that it is the bonds which are formed and broken and must pass through bond lengths which are inappropriate to normal bonds, are the ones which contain most of the weakness of bonding in the transition state.

Substitution at a Singly-unsaturated Carbon Atom.—The transition state must in this case involve a 4-co-ordinated carbon atom and planar square or tetrahedral arrangements of the bonds are therefore reasonable alternatives. The planar structure may be written as (II), (where A is some atom which can be doubly bound to carbon, and i, j is the representation for some unsymmetrical attachment to A) with the entering and ejected groups again tending to be collinear with the central carbon atom. By analogy with the case of substitution at a saturated carbon atom, this is the structure generally assumed for the transition state for ester hydrolysis and similar reactions. The corresponding hybridisation would be *sp* for the collinear R–C–A σ-bonds, one *p*-electron would take part in the formation of the π-bond between C and A, and the remaining *p*-electron would again be contributed towards the weak links to the two groups involved in the substitution.

The extreme alternative structure is a regular tetrahedral disposition of the groups about the central carbon atom. As it is unlikely that a *p*-electron could effectively help to bind three nuclei which are far from collinear, it is probable that the usual sp^3 hybridisation would apply, the bond C–A assuming single-bond character (see figure).

It is of course possible and, in fact, probable that the true state of affairs lies somewhere between these two extremes. It is important to note that the relative contributions of the two forms towards the real structure * may in principle be assessed by stereochemical experiments and that a discussion of this problem is not fundamentally unverifiable. The planar transition state would lead to complete *geometrical* inversion during the reaction, *i.e.*, conversion of (III) into (IV). In the tetrahedral structure, the bond C–A is single and free to rotate, apart from

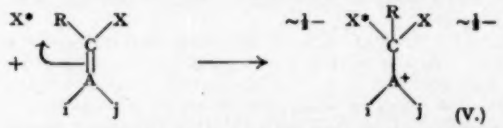
factors outside the bond which may impede or prevent this rotation. The regular tetrahedral transition state should therefore lead to an equilibrium mixture of the isomers. If it is true

* The terms " resonance " or " mesomerism " between the two forms should be used with caution since the forms differ, not only with respect to their electron distributions, but also with respect to the position of the nuclei.

that this structure makes an appreciable contribution (*i.e.*, that the transition state is non-planar) it can be predicted that the geometrical inversion accompanying these reactions will not be complete. So far, substitution reactions involving the replacement of X do not seem to have been observed in cases where i ≠ j and where this test would be possible. Only few cases of substitution in vinyl systems are known, and their mechanism is uncertain (cf. Taft, *J. Amer. Chem. Soc.*, 1949, **70**, 3364). The most important group of substitution reactions at singly unsaturated carbon atoms is that of carbonyl compounds, such as the hydrolysis reactions of esters, acid chlorides, and anhydrides and, naturally, in this group no configurational evidence concerning the steric course of the reaction is possible.

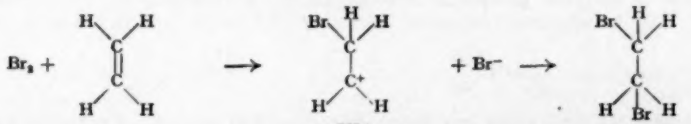
The formulation of the tetrahedral structure may be discussed a little further. The electrical nature of the reagent will determine how single-bond character is acquired by the bond C–A. If X• is nucleophilic (*i.e.*, supplies its own electron pair towards bond formation, like OH^- or R_3N) the Pauli principle will require a pair of electrons to leave the shell of the carbon atom and in the simplest case they will become localised on the atom A, *i.e.*,

(the charges being relative to the initial electrification of the reagents). It is known that carbon has a low electron affinity and this rarely permits the formation of negative ions of the type $\bar{C}R_3$, whereas oxygen-containing anions $\bar{O}R$ are very stable. For this reason the fact that vinyl compounds (A = carbon) undergo nucleophilic substitution reactions only with the greatest difficulty, in contrast to the facility of such reactions for carbonyl compounds (Aij = oxygen), may perhaps be advanced as an argument for the importance of the contribution of the tetrahedral transition-state structure in which the necessity for such a charge separation occurs. Dewar ("Electronic Theory of Organic Chemistry," Oxford, 1949, p. 117) has dismissed the tetrahedral transition state in favour of the planar one for the case of ester hydrolysis, on the grounds that its formation would involve a prohibitive loss of resonance energy, and has stated that the particular reactivity of carbonyl compounds is due to the interaction of the *p*-electrons of the entering and ejected groups with the C=O π-orbital, *i.e.*, that these groups are linked to the central carbon atom by ***partial double*** bonds. However, such conjugation would be more and not less likely in the case of the unreactive vinyl compounds—since C=O π-bonds are more localised than C=C π-bonds (Coulson, *Trans. Faraday Soc.*, 1946, **42**, 106)—so that this factor by itself is an unlikely explanation of the reactivity of esters and related compounds.



(V.)

Conversely, electrophilic reagents would produce the transition state (V), a structure which should be feasible when A is a carbon atom but less favourable for carbonyl compounds. The formula will be recognised also as a more general representation of the labile intermediate formed during the two-stage addition reactions of olefins, *e.g.*,



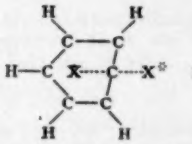
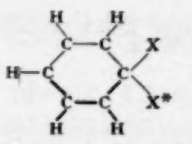
(VI.)

for a review see Gwyn Williams, *Trans. Faraday Soc.*, 1941, **37**, 755). Since it is known that these intermediates are molecular species capable of independent, albeit short-lived, existence, the most stable configuration of (V) will also have this property, *i.e.*, *it* cannot be the transition

state (cf. Taft, *loc. cit.*). The intermediate corresponds to a potential hollow near the saddle-point for the energy profile of the substitution reaction. In the cases where this hollow exists, the transition state of the substitution reaction is the most energised configuration during the formation or decomposition of the intermediate, but inasmuch as the saddle-point is not far removed from the hollow, the *main* valency directions will be the same in the two cases. For reactions in which such an intermediate is formed, the final product should always be the equilibrium mixture of the geometrical isomers, and a measurement of the contribution of the planar form is not possible, but in this case it would not be expected to be important since the intermediate has a tetrahedral structure.

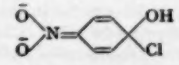
Whether the labile intermediate of the formula (VI) will complete reaction by elimination of one of the groups X or by addition of another group on the opposite side of the double bond is quite irrelevant in this connection. We may also note that a potential hollow near the saddle-point, corresponding to an intermediate, has been established in only a few cases (as in the two-stage halogen addition or the unimolecular elimination reactions (*E*1) and, for instance, there is no evidence for its existence in nucleophilic substitution reactions.

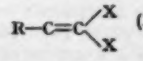
Substitution at an Aromatic Carbon Atom.—This is really a sub-group of the previous class of substitution reactions, the initial hybridisation being the same trigonal sp^2 arrangement. However, the discussion is simpler in this case, since the strict analogue (VII) of the first alternative structure of the last section is planar and clearly sterically impossible and need not be considered further.

(VII.)   (VIII.)

A tetrahedral structure has often, in the past, been assumed for this transition state (VIII) and, indeed, would appear to be the only one possible for a bimolecular aromatic substitution reaction, by whatever type of reagent (Hughes, Ingold, *et al.*, *J.*, 1941, 608). It involves the destruction of the benzene ring conjugation, the conjugated system left over being a pentadienyl frame bearing the appropriate electric charge according to whether the groups X, X* donate, accept, or supply a share of the bonding electrons. Wheland's calculations (*J. Amer. Chem. Soc.*, 1942, **64**, 900) of the stability of the transition state for different kinds of aromatic substitution are based on this assumption (see also Waters, *J.*, 1948, 727, and Dewar, *J.*, 1949, 463). The electrical repulsion between entering and ejected groups may somewhat widen the angle between these bonds, although the resulting utilisation of the electrons would necessarily be less complete, and for this reason we may probably discount a transition state in which approach and ejection of the groups take place in the direction at right angles to the plane of the benzene ring. The hybridisation would in this case be either *sp* for the collinear X–C–X* bonds and *p* σ-bonds to the neighbouring carbon atoms in the ring, or else X–C–X* could be bound by a single *p*-electron, leaving the trigonal sp^2 hybridisation for the two bonds in the ring and the third trigonal orbital unused.

Since the electric charge must, in the tetrahedral transition state, reside on an atom other than those becoming attached to or detached from the benzene ring, nucleophilic substitution occurs only in those benzene derivatives where a better location than a carbon nucleus is available for it, as in *p*-chloronitrobenzene (but not in the *m*-derivative) where structures such as (IX) will be important. On similar reasoning, the chlorine atom in chloroquinones should be hydrolysable.

(IX.) 

 (X.)

The considerations of the last section concerning the occurrence of addition reactions are valid. We may quote one small item of evidence which suggests that the formation of a labile reaction *intermediate* [analogous to (VI)] may occur in certain substitution reactions. Price and Arntzen (*J. Amer. Chem. Soc.*, 1938, **60**, 2835) have shown that bromine addition and the replacement of hydrogen by bromine in aromatic hydrocarbons follow the same unusual kinetic law, from which they concluded that the rate-determining stage was in each case the formation of a cation intermediate. In terms of energy surfaces, the problem whether the proton

abstraction in aromatic nitration *is* (Bennett, Brand, James, Saunders, and Williams, *J.*, 1947, 474) or *is not* (Hughes, Ingold, and Reed, *J.*, 1950, 2428) kinetically significant is then equivalent to the question whether the pass between the " products valley " and the saddle hollow, or that between the " reactants valley " and the saddle hollow is higher in any one particular case.

Substitution at an Acetylenic Carbon Atom.—The *only* feasible structure of the transition state—charge designations being again omitted—is in this case (X), but here again most reagents bring about addition rather than substitution.

A Classification.—The possible transition-state structures may be divided into two extreme classes: (i) those in which a *p*-electron is involved in three-centre binding (called, for brevity, a $p\theta$ electron) and, therefore, increased *s*-character in the remaining valencies, and (ii) those in which the groups involved in substitution are held by near-normal valencies, when the multiplicity of one bond is reduced (the effect may be relayed by conjugation to other bonds) and the *p*-character of the remaining σ-valencies is increased, as summarised in the table.

	Transition-state hybridisation:	
Initial hybridisation.	(i).	(ii).
sp^3	$(sp^2) \cdot p\theta$	—
$sp^2 \cdot p\pi$	$(sp) \cdot p\pi \cdot p\theta$	(sp^3)
$sp \cdot (p\pi)^2$	—	$(sp^2) \cdot p\pi$

The author's thanks are due to Professor E. D. Hughes, F.R.S., and Dr. D. P. Craig for helpful criticism.

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330. *The Reaction of α-Bromobenzyl Cyanide with Ethyl Xanthamidate (Thioncarbamate).*

By W. DAVIES and J. A. MACLAREN.

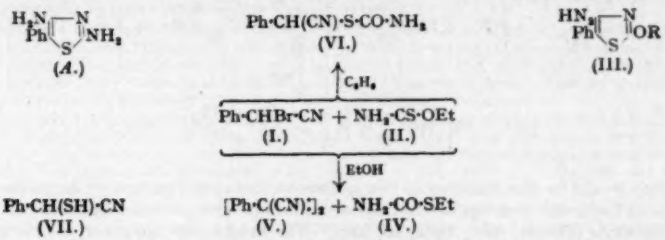
Reaction of α-bromobenzyl cyanide and ethyl xanthamidate, $NH_2 \cdot CS \cdot OEt$, in benzene or without a solvent yields α-carbamylthiobenzyl cyanide (VI), whereas in alcohol the ethyl xanthamidate is isomerized to ethyl thiolcarbamate (IV). The reaction in benzene in the presence of sodium acetate gives 2 : 5-di-(2-ethoxy-5-phenyl-4-thiazolylimino)-3 : 4-diphenylpyrroline (VIII), a brilliant red pigment, of which the structure has been proved by hydrolysis. The synthesis of similar pigments also occurs when methyl and *n*-butyl xanthamidates are used.

THE interaction of α-bromobenzyl cyanide (I) and thiourea has been shown to yield the hydrobromide of 2 : 4-diamino-5-phenylthiazole (*A*) (Davies, Maclaren, and Wilkinson, *J.*, 1950, 3491). Attempts have now been made to extend this reaction by using ethyl xanthamidate (ethyl thioncarbamate) (II) instead of thiourea, and thus to obtain 4-amino-2-ethoxy-5-phenylthiazole (III; R = Et). However, the interaction of (I) and (II) was found to follow three different courses according to the experimental conditions.

In alcoholic solution, (I) and (II) afford ethyl thiolcarbamate (IV), diphenylmaleidinitrile (V), and some ammonium bromide. Various reagents are known to isomerize (II) to (IV); and, as Knorr (*Ber.*, 1917, **50**, 767) and Bettschart and Bystrzicki (*Helv. Chim. Acta*, 1919, **2**, 118) have shown, a trace of an alkyl halide can bring about rearrangements of this type. Hence (I) is probably the effective agent in this case. It is known that α-bromobenzyl cyanide gives (V) when treated with weak bases, when heated, or when kept for a long time (Kinnear, *J. Soc. Chem. Ind.*, 1948, **67**, 35), and the ammonium bromide must result from partial hydrolysis.

When ethyl xanthamidate and α-bromobenzyl cyanide are heated together alone, or in benzene solution, a compound $C_9H_8ON_2S$ (m. p. 105—106°) is formed. Since it cannot be desulphurized by the usual reagents, it might be regarded as either α-carbamylthiobenzyl cyanide (VI) or 2-hydroxy-4-amino-5-phenylthiazole (III; R = H). From the ready fissions

which it undergoes, the acyclic structure (VI) seems to be correct. With mercuric chloride solution it gives the mercuric salt of α-mercaptobenzyl cyanide (VII). The derived free thiol has been described by Kretow and Pantschenko (*Chem. Zentr.*, 1930, I, 3551), but the details in



(A.)

(III.)

the abstract are so vague that all our attempts to prepare this probably unstable compound have been unsuccessful. The above reaction of mercuric chloride, however, is now found to be general with thiolcarbamates and apparently proceeds thus :

$$2R{\cdot}S{\cdot}CO{\cdot}NH_2 + HgCl_2 \longrightarrow (R{\cdot}S)_2Hg + 2CO_2 + 2NH_4Cl$$

With aniline, the compound gives an unidentified thiol and *s*-diphenylurea; *p*-anisidine similarly gives *s*-di-(*p*-methoxyphenyl)urea. These are examples of a recognized general reaction (Blankenhorn, *J. pr. Chem.*, 1887, [ii], **16**, 375) :

$$R{\cdot}S{\cdot}CO{\cdot}NH_2 + 2R'{\cdot}NH_2 \longrightarrow (R'{\cdot}NH)_2CO + R{\cdot}SH + NH_3$$

Finally, the compound (m. p. 105—106°) is hydrolysed by alkaline solutions to the dinitrile (V), and this and the two previous reactions support the structure (VI) rather than (III). The observation that acid hydrolysis gives 2 : 4-dihydroxy-5-phenylthiazole (X) might seem to indicate structure (III; R = H), at least in acid solution. This assumption, however, is not essential since acid hydrolysis of α-thiocyano-esters and amides is known to give the corresponding 2 : 4-dihydroxythiazoles (*e.g.*, Wheeler and Barnes, *Amer. Chem. J.*, 1900, **24**, 80).

The formation of (V) on interaction of (VI) and alkali recalls its similar formation from α-bromobenzyl cyanide. There are other known instances where a potential anion (usually halogen) is removed as an alkali salt and an ethylenic compound formed; for example, ethyl α-bromophenylacetate with alkali gives diethyl diphenylmaleate (Ramart-Lucas and Hoch, *Ann. Chim.*, 1943, [x], **18**, 390), and similarly ethyl bromomalonate yields ethyl ethylenetetracarboxylate; also, in the benzyl chloride series, the nitro- and cyano-derivatives yield the corresponding disubstituted stilbenes (Weygand, " Organic Preparations ", Interscience Publ., New York, 1945, p. 417).

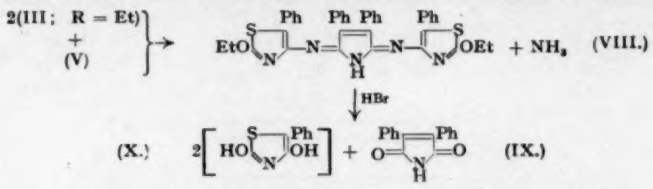
The absence of ring closure of the carbamylthiol (VI) is in contrast to the behaviour of the corresponding *iso*thiourea hydrobromide, which cannot be isolated since it is rapidly converted into the hydrobromide of 2 : 4-diamino-5-phenylthiazole (*A*) (Davies, Maclaren, and Wilkinson, *loc. cit.*). The weakly basic nature of the S·CO·NH$_2$ group in (VI) is in contrast to the strongly basic *iso*thiourea group and may be responsible for the lack of ring formation.

It seems likely that (VI) results by de-ethylation of the initially formed

Ph·CH(CN)·S·C(:NH)·OEt

which, being a stronger base than (VI), might cyclize to form 4-amino-2-ethoxy-5-phenylthiazole (III; R = Et). Hantzsch (*Ber.*, 1927, **60**, 2537) has shown that, in the similar condensation of ethyl xanthamidate with chloroacetone, de-ethylation may be avoided by neutralizing the acid formed with potassium acetate. Accordingly ethyl xanthamidate and (I) have been condensed in the presence of sodium acetate, but instead of the expected primary reaction product (III; R = Et), much resinous matter and a bright red crystalline product $C_{34}H_{31}N_5S_2(OEt)_2$ were isolated. This compound is remarkably stable to heat and to the usual acid and alkaline reagents and hence probably has value as a pigment. It is, however, hydrolysed quantitatively by hydrobromic acid in acetic acid to yield ethyl and ammonium bromides, diphenylmaleinimide (IX), and 2 : 4-dihydroxy-5-phenylthiazole (X), the last two in the approximate molar ratio of 1 : 2. Hence 2 : 5-di-(2-ethoxy-5-phenyl-4-thiazolylimino)-3 : 4-diphenylpyrroline (VIII) is accepted as the structure of the pigment, in which the complete conjugation explains the intense colour. Methyl and *n*-butyl xanthamidates give the corresponding alkoxy-

homologues of (VIII) as crystalline solids. The synthesis is probably due to the union of one molecule of (V) with two molecules of the intermediate (III; R = Et), thus:



The first step would be the addition of the amino- to the cyano-groups to form the diamidine derivative. This could then cyclize by loss of ammonia, just as succindiamidine is converted into succinimidine (Pinner, *Ber.*, 1883, **16**, 352). The mechanism, however, is obscure since no pigment is formed when (V) is heated with sodium acetate and salts of 2-amino- and 2 : 4-diamino-thiazole.

The scope of this synthesis has been shown by qualitative test-tube reactions. When samples of the reagents listed below are mixed with approximately equal amounts of α-bromobenzyl cyanide and sodium acetate and heated, the following colour changes (in parentheses) are observed: thiourea (red-brown); *N*-phenylthiourea (purple); benzamidine hydrochloride, 2-amino-thiazole, 2-aminopyridine, and 2-4-diaminothiazole (red). Presumably the thioamide is first converted into the 4-aminothiazole derivative (Davies, Maclaren, Wilkinson, *loc. cit.*); it is seen that, with the exception of guanidine nitrate (which yields a brownish colour), all compounds containing the group ·C(:NH)·N: give an intensely coloured reaction mixture. Unfortunately in these cases the pigment has not been isolated, owing to the simultaneous formation of tar, which has defeated all attempts at recrystallization.

These polynuclear heterocyclic compounds (*e.g.*, VIII) are closely comparable with the tetra-arylazadipyrromethines (Rogers, *Nature*, 1943, **191**, 504; *J.*, 1943, 590). The structure of (VIII) also recalls that of the octaphenylporphyrazines, of which the metallic derivatives are made by heating (V) with various metals (Linstead and Cook, *J.*, 1937, 929).

Experimental.

Xanthamidates.—Ethyl xanthamidate was prepared by a method based on that of Holmberg (*Chem. Zentr.*, 1930, I, 1925): A solution of sodium hydroxide (20 g.) in water (300 ml.) was shaken with ethyl alcohol (100 ml.) and carbon disulphide (35 ml.), until dissolution was complete, and then left at room temperature for 1 hour. A solution of sodium hydroxide (20 g.) in water (200 ml.) was neutralized slowly with chloroacetic acid (47 g.) in an ice-bath, and the resulting solution was added to the sodium ethyl xanthate obtained above. After being kept overnight, this mixture was evaporated on the water-bath, at reduced pressure to 150 ml.; aqueous ammonia (30 ml.; *d* 0·88) was added and the mixture kept overnight. After neutralization with acetic acid, the mixture was extracted with ether (3 × 100 ml.), which after being dried (Na_2SO_4) and evaporated, yielded colourless plates (31 g., 58%), m. p. 38—40°, which were sufficiently pure for immediate use. This yield can be maintained even on five times this scale.

Methyl xanthamidate, prepared in the same manner, was obtained as plates, m. p. 42—45° (51%).

n-*Butyl xanthamidate*, obtained similarly, was distilled (b. p. 127—133°/15 mm.); it crystallized as plates, m. p. 16—19° (yield 45%) (Found: N, 10·6. $C_5H_{11}ONS$ requires N, 10·5%).

α-*Bromobenzyl Cyanide.*—The compound used was a redistilled approx. 60% solution of α-bromobenzyl cyanide in benzyl cyanide, prepared originally for chemical warfare purposes. That the benzyl cyanide took no part in the reactions was shown by repeating them on a small scale with pure α-chlorobenzyl cyanide, b. p. 117—118·5°/18 mm. (Hignett and Kay, *J. Soc. Chem. Ind.*, 1935, **54**, 98T, report b. p. 131·5°/13 mm.) (Found: N, 9·6. Calc. for C_8H_6NCl: N, 9·3%).

Interaction of α-Bromobenzyl Cyanide and Ethyl Xanthamidate.—Equimolar amounts of (I) and (II) in ethyl alcohol were refluxed for 3 hours. The precipitate of ammonium bromide (0·05 mol.) was filtered off, and the filtrate on evaporation yielded a white crystalline solid and a brown oil. The solid, after being washed wth methyl alcohol and recrystallized from ethyl alcohol, melted at 162—163°, unchanged by mixing with authentic (V), prepared by Kinnear's method (*loc. cit.*). The brown oil solidified after being kept in a vacuum-desiccator and crystallized from benzene–light petroleum as plates, m. p. 102·5—103·5° (Found: N, 13·6. Calc. for C_9H_7ONS: N, 13·3%). This compound was identified as (IV) by a mixed m. p. with an authentic sample (Wheeler and Barnes, *Amer. Chem. J.*, 1899, **22**, 148). The reaction was the same when the above reaction mixture was kept at 40° for 5 days.

Equimolar amounts of (I) and (II) were refluxed in benzene for 3 hours, and the solvent was then removed on the water-bath; the reaction mixture, on cooling, deposited α-*carbamylthiobenzyl cyanide* as a crystalline solid, which recrystallized from benzene–light petroleum as needles (56%), m. p. 105—106° (Found: C, 56·6; H, 4·2; C, 17·1. $C_9H_8ON_2S$ requires C, 56·3; H, 4·2; S, 16·7%).

The same product was obtained by warming an equimolar mixture of the reactants until dissolution was complete and then storing them at 40° for 10 days.

This product was soluble in alcohol and aqueous alkali but insoluble in aqueous acid; it could not be diazotized or acetylated by the usual methods, and treatment with phenyl *iso*cyanate yielded only carbanilide, probably owing to presence of a trace of water.

Hydrolysis of α-Carbamylthiobenzyl Cyanide.—Acid hydrolysis resulted when the cyanide (0·5 g.) was refluxed in ethyl alcohol (5 ml.) and concentrated hydrochloric acid (5 ml.) for 2 hours. The mixture was evaporated to about half its volume, then diluted with water, and, on cooling, a precipitate formed which recrystallized from water as needles, m. p. 132—133° alone or mixed with an authentic sample of 2 : 4-dihydroxy-5-phenylthiazole (Davies, Maclaren, Wilkinson, *loc. cit.*).

Alkaline hydrolysis resulted when sodium (0·05 g.), dissolved in methyl alcohol (15 ml.), and the cyanide (VI) (0·5 g.) were kept at room temperature for 2 days. The pale brown solution was then filtered and the long needles were washed with a small volume of carbon disulphide and recrystallized from alcohol. The diphenylmaleidinitrile (0·2 g.) had m. p. 162—163°. The filtrate and wash-liquor contained sulphur and other unidentified products.

Hydrolytic fission occurred in a third manner in the presence of mercuric chloride. Solutions of the cyanide (VI) (0·5 g.) in ethyl alcohol (5 ml.) and of mercuric chloride (0·7 g.) in water (30 ml.) were mixed, and the mixture was heated to boiling, cooled, and filtered. The product which crystallized from aqueous alcohol as colourless plates, m. p. 159—160°, was the *mercuric* salt of α-mercaptobenzyl cyanide (Found : C, 38·7; H, 2·5; N, 5·5. $C_{16}H_{12}N_2S_2Hg$ requires C, 38·8; H, 2·4; N, 5·6%).

Methyl thiolcarbamate (0·2 g.) was dissolved in hot water and saturated mercuric chloride solution (20 ml.) was added. The resulting white precipitate was coagulated by boiling for 5 minutes; recrystallized from aqueous pyridine, *chloromercurithiomethane* melted above 300° (Found : C, 4·8; H, 1·4; S, 11·15. CH_2SClHg requires C, 4·2; H, 1·1; S, 11·3%).

Reaction of α-Carbamylthiolbenzyl Cyanide with Amines.—When equal weights of the cyanide and aniline were heated together, ammonia was evolved and the mixture became semisolid. After cooling, the mixture was filtered and the product washed with 50% acetic acid and crystallized from alcohol as needles, m. p. 237—238°, identical with *s*-diphenylurea. Under the same conditions, *p*-anisidine gave *s*-di-(*p*-methoxyphenyl)urea as needles (from alcohol), m. p. 236—237°, (Found : OMe, 22·9. Calc. for $C_{15}H_{16}O_3N_2$: OMe, 22·8%). Lossen (*Annalen*, 1875, **175**, 295) describes this substance as melting at 234—235°.

3 : 4-*Diphenyl*-2 : 5-*di*(*thiazolylimino*)*pyrroline Derivatives.*—In preliminary experiments, equimolar quantities of (I), (II), and sodium acetate were heated together on a water-bath for 5 hours. The mixture rapidly became deep red. The residue after steam-distillation was a black, brittle, thermoplastic resin which could not be crystallized, but in boiling alcoholic hydrochloric acid yielded some 2 : 4-dihydroxy-5-phenylthiazole, m. p. 130—132°. (II) (10·5 g.), (I) (40 ml. of 60%), and anhydrous sodium acetate (18 g.) were refluxed in benzene (60 ml.) for 5 hours. The reaction mixture was filtered and the precipitate was washed with hot benzene until colourless. The solvent was then evaporated from the filtrate and washings, and the last traces were removed on the water-bath at reduced pressure. The resulting red-black mixture was filtered and the precipitate was repeatedly crystallized from benzene as brilliantly red needles, m. p. 222·5—223°, of 2 : 5-*di*-(2-*ethoxy*-5-*phenyl*-4-*thiazolylimino*)-3 : 4-*diphenylpyrroline* (6 g., 10%) [Found : C, 69·2; H, 5·0; N, 10·6; S, 10·0; OEt, 13·95. $C_{34}H_{31}N_5S_2(OC_2H_5)_2$ requires C, 69·9; H, 4·8; N, 10·7; S, 9·8; OEt, 13·8%]. The product was soluble in hot chloroform, benzene, or dioxan, sparingly soluble in alcohol or acetone, and insoluble in water, light petroleum, aqueous acids or alkalis. It did not react with the usual acids and alkalis, but was hydrolysed by hydrobromic acid in acetic acid as follows.

The pyrroline (1 g.) in concentrated hydrobromic acid (1 ml.; *d* 1·70) and acetic acid (5 ml.) was heated to boiling, the solution being rapidly decolorized and finally becoming deep yellow. The solution was evaporated to dryness at reduced pressure, and the residue was treated with water (50 ml.). The resulting yellow precipitate was filtered off. Repeated extraction with boiling water separated the soluble 2 : 4-dihydroxy-5-phenylthiazole (0·40 g., 68%) from the insoluble diphenylmaleinimide (0·38 g., 99%). The former product crystallized from water as needles, m. p. and mixed m. p. 131—132°. The structure of the imide, which crystallized from alcohol as yellow needles, m. p. 217—218° (lit., 217°), was established by analyses (Found : C, 77·5; H, 4·7; N, 5·9. Calc. for $C_{16}H_{11}O_2N$: C, 77·1; H, 4·4; N, 5·6%) and by alkaline hydrolysis to diphenylmaleic anhydride.

2 : 5-*Di*-(2-*methoxy*-5-*phenyl*-4-*thiazolylimino*)-3 : 4-*diphenylpyrroline* was obtained in a similar manner by using methyl xanthamidate, and formed red needles (12%), m. p. 277—278°, from benzene [Found : C, 69·05; H, 4·2; N, 11·6; S, 10·2; OMe, 9·9. $C_{34}H_{31}N_5S_2(OCH_3)_2$ requires C, 69·2; H, 4·3; N, 11·2; S, 10·2; OMe, 9·9%].

2 : 5-*Di*-(2-n-*butoxy*-5-*phenyl*-4-*thiazolylimino*)-3 : 4-*diphenylpyrroline*, prepared from *n*-butyl xanthamidate, formed red needles (11%) (from acetic acid), m. p. 205—205·5° (Found : C, 71·2; H, 5·6; N, 9·8; S, 9·1. $C_{42}H_{39}O_2N_5S_2$ requires C, 71·1; H, 5·5; N, 9·9; S, 9·0%).

Molecular weight determinations. The Rast method was not applicable as the solutions obtained were too intensely coloured. However, the molecular weight of the ethoxy-derivative as determined by Clarke's isothermal distillation method (*Ind. Eng. Chem.*, 1941, **13**, 820), using chloroform as solvent and stilbene as standard, was 651 ± 6 ($C_{38}H_{31}O_2N_5S_2$ requires *M*, 653).

Micro-analyses were carried out under the direction of Dr. W. Zimmermann and Mr. N. L. Lottkowitz. The authors thank the Commonwealth National Health and Medical Research Council for a research grant.

UNIVERSITY OF MELBOURNE. [*Received, January 29th*, 1951.]

331. *The Ultra-violet Absorption Spectra of Mercurous Perchlorate Solutions.*

By W. C. E. Higginson.

The marked ultra-violet light absorption of the dimeric mercurous ion in the wave-length range 200—300 mμ. enables concentrations of mercurous perchlorate down to 3×10^{-6}M. to be determined in dilute perchloric acid solutions by means of a spectrophotometer.

It is suggested that deviations from Beer's law, which become apparent at concentrations below 10^{-6}M-mercurous perchlorate, show a significant degree of dissociation of the dimer at these concentrations, leading to a value of $K_{diss.} = [Hg^+]^2/[Hg_2^{++}]$ within the limits 10^{-5} and 10^{-4}.

In an attempt to find a simple method for estimating concentrations of mercurous mercury as low as 10^{-5}M., the absorption spectrum of mercurous perchlorate in dilute perchloric acid was investigated. Considerable absorption was found in the wave-length range 200—300 mμ., with absorption maxima at 209 and 236·5 mμ., corresponding to those observed for the sulphate at 214 and 240 mμ. (Kato, *Bull. Inst. Phys. Chem. Res. Japan*, 1930, **12**, 230). The molecular extinction coefficient at 236·5 mμ. (the more pronounced maximum) was found to be of the order $2{\cdot}8 \times 10^4$ and was thus sufficiently large to justify further investigation of the possibilities of this method.

Experimental.

Reagents were of AnalaR quality unless otherwise stated. Metallic mercury was purified by drawing air through the metal for several days, followed by passage through columns of dilute nitric acid and distilled water, and finally by distillation under reduced pressure. Silver perchlorate was prepared from AnalaR materials by Hill's method (*J. Amer. Chem. Soc.*, 1921, **43**, 254).

Mercurous perchlorate solution, 0·0509M. in mercurous perchlorate and 0·0341M. in perchloric acid, was prepared and standardised against 0·0594M-sodium chloride solution by use of bromophenol-blue as adsorption indicator (Pugh, *J.*, 1937, 1824). This stock solution was kept over a few grams of metallic mercury. A more dilute stock solution, prepared by dilution of the 0·0509M-mercurous perchlorate solution with dilute perchloric acid, was standardised potentiometrically against $1{\cdot}484 \times 10^{-2}$M-sodium chloride solution (Müller and Aarflot, *Rec. Trav. chim.*, 1924, **43**, 874). This solution, $5{\cdot}10 \times 10^{-4}$M. in mercurous perchlorate and $1{\cdot}04 \times 10^{-2}$M. in perchloric acid, was not kept in contact with metallic mercury, but nevertheless remained unaltered for 4 months as shown by subsequent titration, and also by the constant optical density at 236·5 mμ. of samples diluted ten times.

Perchloric acid solutions were standardised against standard baryta with bromothymol-blue as indicator. The perchloric acid (60%) used was shown by potentiometric titration against mercurous perchlorate to contain approximately 7×10^{-4} mole of chloride ion per mole of perchloric acid. In mercurous perchlorate solutions of concentration 3×10^{-6}M. and above, this impurity had no noticeable effect on the optical density up to a concentration of about 0·05M-perchloric acid, *i.e.*, $[Cl^-] = 3{\cdot}5 \times 10^{-5}$M. At higher perchloric acid concentrations, or at mercurous concentrations of the order of 10^{-6}M. and less, even with 10^{-2}M-perchloric acid, there was an appreciable diminution in the expected optical density when the untreated acid was used, presumably owing to the formation of calomel or a chloride complex. For measurements at these concentrations, perchloric acid of lower chloride-ion content was prepared by the addition of sufficient silver perchlorate solution to give an excess of $3{\cdot}2 \times 10^{-4}$M. of silver ion in a 9M-perchloric acid solution. Vigorous shaking coagulated the silver chloride precipitate, which was removed by passing the solution through a No. 3 sintered-glass filter. The treated solutions thus contained $3{\cdot}5 \times 10^{-5}$ mole of silver perchlorate per mole of perchloric acid, and the chloride ion remaining, the silver chloride solubility product in 9M-perchloric acid being assumed equal to that in water, was of the order 6×10^{-9} mole per mole of perchloric acid.

A solution of Hopkin and Williams's sodium perchlorate was treated similarly, and the resulting solutions contained $1{\cdot}7 \times 10^{-4}$ mole of silver perchlorate per mole of sodium perchlorate. The proportion of chloride ion remaining was again of the order 6×10^{-9} mole per mole of sodium perchlorate. These treated perchloric acid or sodium perchlorate solutions were employed in all cases where their use, as compared with untreated solutions, was found to cause an appreciable alteration in the optical density, *i.e.*, in those instances referred to above.

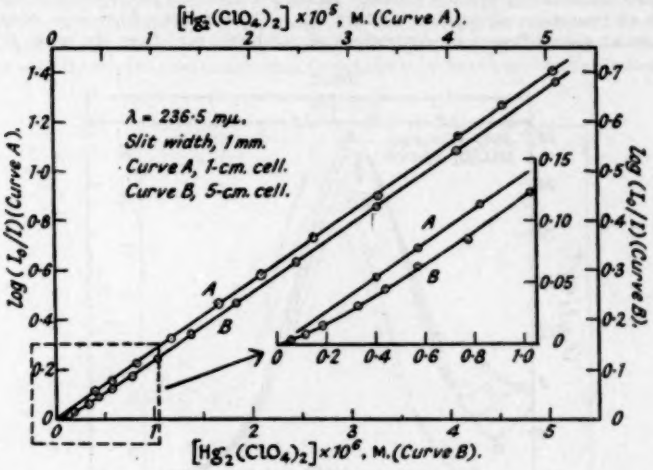
The spectrophotometers used were, for 1-cm. optical length cells a Unicam model SP 500 quartz spectrophotometer, and for 5-cm. cells a Beckman model DU quartz spectrophotometer. Measurements were made at room temperature, approximately 18°.

Results and Discussion.

Optical-density Measurements as a Method of determining Mercurous Perchlorate Concentrations.—The highest concentration of mercurous perchlorate for which the full molecular extinction curve between 200 and 300 mμ. can satisfactorily be determined with a cell of 1-cm.

optical length is of the order 5×10^{-5}M., and the corresponding optical density at the most pronounced absorption maximum ($\lambda = 236{\cdot}5$ mμ.) is approximately 1·4. At this wave-length Beer's law is apparently obeyed over the concentration range $[Hg_2(ClO_4)_2] = 5 \times 10^{-6}$—$3 \times 10^{-4}$M.; $[HClO_4] = 10^{-2}$M. (Fig. 1, curve *A*). Similar measurements at concentrations of perchloric acid between 10^{-3}M. and 10^{-1}M. gave, for corresponding concentrations of mercurous perchlorate, values of the optical density identical within experimental error. The addition of sodium perchlorate up to a concentration of 10^{-1}M. ($[HClO_4] = 10^{-2}$M.) also caused no observable change. The value of $\varepsilon_{obs.}$ at 236·5 mμ. under these conditions is $(2{\cdot}78 \pm 0{\cdot}02) \times 10^4$.

FIG. 1.



To extend the concentration range of mercurous perchlorate which can be determined, plots of $\log(I_0/I)$ against $[Hg_2(ClO_4)_2]$ (*c*) were constructed from measurements at longer wave-lengths. In all cases these plots were linear and passed through the origin; the results are

TABLE I.

λ(mμ.).	$Hg_2(ClO_4)_2$, concn. range (moles per l.).	$\varepsilon_{obs.} = \log(I_0/I)/cl.$*	Slit width, mm.	$[HClO_4]$ (moles per l.).
295	$5{\cdot}1 \times 10^{-5}$—$2{\cdot}0 \times 10^{-4}$	30·4	0·5	$3{\cdot}4 \times 10^{-2}$
275	$5{\cdot}6 \times 10^{-5}$—$1{\cdot}6 \times 10^{-4}$	254	0·5	$3{\cdot}4 \times 10^{-2}$
260	$4{\cdot}4 \times 10^{-4}$—$2{\cdot}0 \times 10^{-3}$	3480	1·0	$3{\cdot}4 \times 10^{-2}$
254	$1{\cdot}6 \times 10^{-4}$—$7{\cdot}3 \times 10^{-3}$	8500	1·0	$3{\cdot}4 \times 10^{-2}$
236·5	$5{\cdot}1 \times 10^{-6}$—$3{\cdot}0 \times 10^{-5}$	$(2{\cdot}78 \pm 0{\cdot}02) \times 10^4$	1·0	10^{-2}—10^{-1}

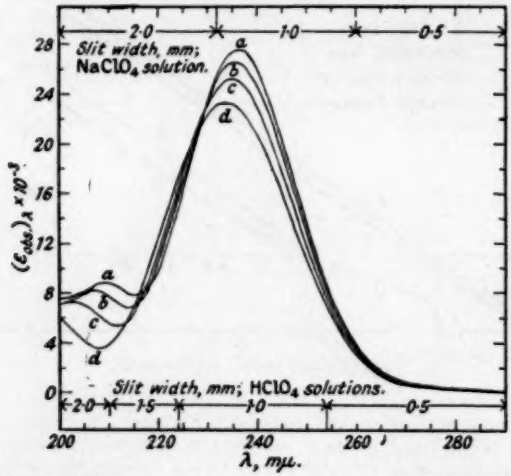
* Optical length of cell, 1 cm.

summarised in Table I. The values of $\varepsilon_{obs.}$ except at 236·5 mμ. are probably not accurately reproducible from one instrument to another, as in this part of the spectrum the molecular extinction increases rapidly with decreasing wave-length, and the wave-length calibration of a spectrophotometer may differ from the true value by as much as 0·5 mμ. in this region. Nevertheless, for a given wave-length setting and slit width of a particular instrument, the use of longer wave-lengths than 236·5 mμ. enables the range of concentrations which can be determined to be increased up to 5×10^{-3}M-mercurous perchlorate, provided that the concentration can be found in one instance by another method.

The Effect of Acid Strength and Salt Concentration on $\varepsilon_{obs.}$.—At concentrations of perchloric acid smaller than 10^{-3}M., the value of $\varepsilon_{obs.}$ at 236·5 mμ. was found to be less than $2{\cdot}78 \times 10^4$, the effect increasing with decreasing acidity. This was not investigated in detail but is probably due to the formation of a hydroxyl complex.

Above concentrations of 10^{-1}M. of added perchloric acid or sodium perchlorate there is a small effect of salt concentration on the molecular extinction curve. Fig. 2 shows plots of $(\varepsilon_{obs.})_\lambda$ against λ for various concentrations of perchloric acid and sodium perchlorate. In addition to a decrease in the value of $\varepsilon_{obs.}$ for the main absorption peak, there is also a small shift of the whole extinction curve to the ultra-violet, most pronounced at the shorter wave-lengths. At the main maximum, the decrease in $\varepsilon_{obs.}$ is linear with concentration and $(\varepsilon_{obs.})_{max.}$ is given for perchloric acid by $(\varepsilon_{obs.})_{max.} = (2{\cdot}78 - 0{\cdot}055[HClO_4]) \times 10^4$, and for sodium perchlorate by $(\varepsilon_{obs.})_{max.} = (2{\cdot}78 - 0{\cdot}035[NaClO_4]) \times 10^4$, the concentrations being expressed in moles per litre. The corresponding movement of the wave-length is also linear in concentration, and the position of the absorption maximum varies from 236·5 mμ. in 10^{-3}—10^{-1}M- to 233·5 mμ. in 8·08M-perchloric acid. In the presence of 4·38M-sodium perchlorate, the wave-length of maximum absorption is 235·5 mμ. These relationships were obtained from measurements at nine different concentrations of perchloric acid over the range 0·1—8·08M.,

FIG. 2.



(*a*) 0·05M-$HClO_4$. (*c*) 4·49M-$HClO_4$.
(*b*) {1·80M-$HClO_4$ and 2·90M-$NaClO_4$, $1{\cdot}04 \times 10^{-3}$M-$HClO_4$. (*d*) 8·08M-$HClO_4$.
$[Hg_2(ClO_4)_2] = 5{\cdot}07 \times 10^{-3}$M. (1-cm. cell).

and at six different concentrations of sodium perchlorate over the range zero to 4·38M. In the latter measurements the perchloric acid concentration was maintained constant at $1{\cdot}04 \times 10^{-3}$M.

As the concentrations of acid or salt added are large, these relatively small effects may be due merely to a change in the physical nature of the solvent medium rather than to chemical association. It thus seems that the light absorption is due to mercurous mercury, and that in the range 10^{-3}—10^{-1}M-perchloric acid at least, the formation of hydroxyl ion or perchlorate ion complexes is negligible. This was partly confirmed by measurements on mercurous nitrate in $1{\cdot}04 \times 10^{-3}$M-nitric acid which gave a value of $(\varepsilon_{obs.})_{236{\cdot}5}$ of $2{\cdot}79 \times 10^4$, and the extinction curve from 300 mμ. to 230 mμ. was similar to that obtained with mercurous perchlorate in $1{\cdot}04 \times 10^{-3}$M-perchloric acid. Below 230 mμ., small discrepancies were observed, but here the absorption due to the nitrate ion becomes considerable, and it was not possible to take measurements below 220 mμ., even at the full slit width of 2 mm.

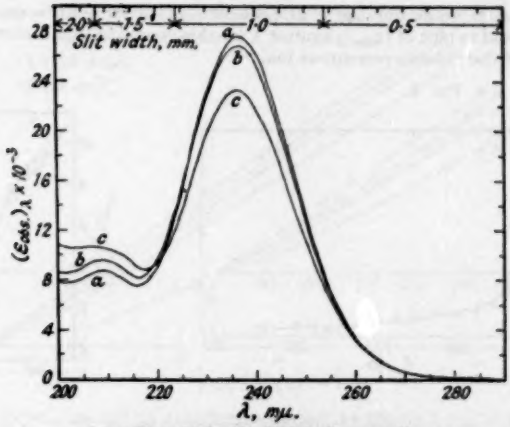
Deviations from Beer's Law.—In an attempt to extend the analytical use of optical-density determinations to concentrations lower than 3×10^{-4}M-mercurous perchlorate, the dependence of $\log (I_0/I)_{236{\cdot}5}$ on mercurous perchlorate concentration was investigated over the concentration range 5×10^{-4}—5×10^{-6}M., a cell of optical length 5 cm. being used. The solutions were made by successive dilutions from a solution $5{\cdot}10 \times 10^{-3}$M. in mercurous perchlorate and $1{\cdot}04 \times 10^{-2}$M. in perchloric acid. The concentration of the latter solution was checked by measuring its

optical density at 236·5 mμ. in a 1-cm. cell. Measurements were made at $1{\cdot}04 \times 10^{-3}$M- and at $1{\cdot}04 \times 10^{-2}$M-perchloric acid (treated with silver perchlorate) and each was repeated with completely new solutions. Agreement between the four sets of measurements was within experimental error. The average values of the optical density at 236·5 mμ. plotted against the concentration are shown in Fig. 1, curve *B*. Fig. 3 shows the plot of $(\varepsilon_{obs.})_\lambda$ against λ for solutions of mercurous perchlorate concentration $5{\cdot}80 \times 10^{-5}$M. (1-cm. cell), $5{\cdot}10 \times 10^{-4}$M., and $1{\cdot}02 \times 10^{-4}$M., severally. The perchloric acid concentration was $1{\cdot}04 \times 10^{-3}$M.

Various factors were considered in an attempt to account for the observed deviations from Beer's law at 236·5 mμ. and for the anomalous character of the $(\varepsilon_{obs.})_\lambda$–λ plots at different concentrations.

(1) Atmospheric oxidation of the mercurous ion does not appear to be responsible, as the optical density of the solutions remained constant over periods in excess of those required to make a complete set of optical measurements. (2) Adsorption of the mercurous ion on the walls of the vessels and cells used could cause deviations from Beer's law similar to those observed,

FIG. 3.



(*a*) $5{\cdot}80 \times 10^{-5}$M-$Hg_2(ClO_4)_2$ (1-cm. cell).
(*b*) $5{\cdot}10 \times 10^{-4}$M-$Hg_2(ClO_4)_2$ (5-cm. cell).
(*c*) $1{\cdot}02 \times 10^{-4}$M-$Hg_2(ClO_4)_2$ (5-cm. cell).
$[HClO_4] = 1{\cdot}04 \times 10^{-3}$M.

but does not lead to a satisfactory explanation of the change in shape of the molecular extinction curves. (3) The establishment of the equilibrium $Hg_2^{++} \rightleftharpoons Hg^{++} + (Hg)_{liq.}$ would lead to linear rather than curved plots of optical density against concentration, and it is doubtful on energetic grounds whether the corresponding equilibrium involving mercury atoms could occur to an appreciable extent. (4) Impurities capable of reacting with mercurous ions and present in the perchloric acid solutions used for dilution could account for the effects observed. Such impurities are unlikely to be present in the silver perchlorate-treated, concentrated perchloric acid, as good agreement was found between measurements in which the perchloric acid concentrations differed ten-fold. The only remaining source seems to be the distilled water used; but samples distilled on different occasions were used with concordant results.

(5) The explanation adopted as most probable is that of an increasing finite degree of dissociation of the dimeric mercurous ion with decrease in total mercurous concentration. If this is the case, the larger values for $(\varepsilon_{obs.})_\lambda$ for the $1{\cdot}02 \times 10^{-4}$M-mercurous perchlorate solution at wave-lengths less than 220 mμ. imply that at these wave-lengths the molecular extinction coefficient of the Hg^+ ion is comparable in magnitude with that of Hg_2^{++}. Thus even at 236·5 mμ. the contribution of the Hg^+ ions present to the total absorption may be significant in the most dilute solution. Comparison of the values of

$$\left(\frac{\varepsilon_{obs.},\ c = 1{\cdot}02 \times 10^{-4}\text{M.}}{\varepsilon_{obs.},\ c = 5{\cdot}80 \times 10^{-5}\text{M.}}\right)_\lambda$$

at different values of λ (Fig. 4) shows that there is an approximate constancy over the range λ = 245—254 mμ., and here this ratio reaches a minimum, 0·82. The possibility that here there is a similar functional dependence of ε_{Hg^+} and $\varepsilon_{Hg_2^{++}}$ on λ seems unlikely. It appears more probable that over this wave-length range the absorption due to Hg^+ is negligible, and in any case there must be a finite absorption due to the monomeric ion at 236·5 mμ. (At wave-lengths greater than 254 mμ. an increase in this ratio is noticeable, but here the experimental error on the $(\varepsilon_{obs.})_\lambda$ values becomes large, *e.g.*, the value of the optical density at a concentration of $1·02 \times 10^{-6}$M. is only 0·016 at 260 mμ.) On the assumption that the degree of dissociation in the $5·80 \times 10^{-5}$M-solution is small

$$\left(\frac{\varepsilon_{obs.},\ c = 1·02 \times 10^{-6}\text{M.}}{\varepsilon_{obs.},\ c = 5·80 \times 10^{-5}\text{M.}}\right)_{245—254} = 1 - \alpha$$

where α is the degree of dissociation in the $1·02 \times 10^{-6}$M-solution. Hence

$$K_{diss.} = \frac{[Hg^+]^2}{[Hg_2^{++}]} = \frac{2^2(1 - 0·82)^2(1·02 \times 10^{-6})^2}{(0·82)\ (1·02 \times 10^{-6})} = 1·6 \times 10^{-7}$$

From this approximate value the degree of dissociation in $5·80 \times 10^{-5}$M-mercurous perchlorate is about 0·02, and so the plot of $(\varepsilon_{obs.})_\lambda$ against λ for this concentration is virtually the molecular extinction curve of the dimeric mercurous ion.

FIG. 4.

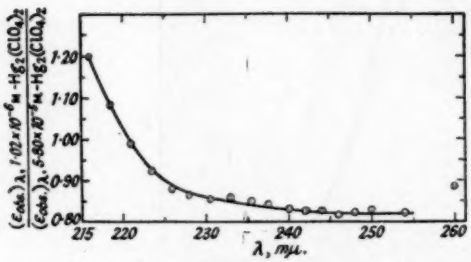
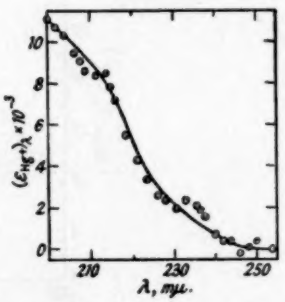


FIG. 5.



In $1·02 \times 10^{-6}$M-mercurous perchlorate the concentration of Hg_2^{++} is $8·4 \times 10^{-7}$M., and of Hg^+ $3·7 \times 10^{-7}$M. Subtraction from the log $(I_0/I)_\lambda$ values for $1·02 \times 10^{-6}$M-mercurous perchlorate of the log (I_0/I) values for $8·4 \times 10^{-7}$M. "pure" dimer (calculated from the molecular extinction coefficients obtained from the $5·80 \times 10^{-5}$M-solution) gives the optical density due to $3·7 \times 10^{-7}$M-Hg^+ ion, and Fig. 5 shows the corresponding molecular extinction curve. Owing to the comparatively small differences between the two sets of figures, and to the approximations made, Fig. 5 gives at best only a semi-quantitative representation of the true molecular extinction curve for Hg^+.

To decide if the shape of the observed plot of log $(I_0/I)_{236·5}$ against mercurous perchlorate concentration (Fig. 1, curve *B*) is consistent with the approximate $K_{diss.}$ value obtained above, curves have been constructed for various values of $K_{diss.}$ by using the expression

$$\log (I_0/I)_{236·5}/l = (\varepsilon_{Hg_2^{++}})_{236·5} \times [Hg_2^{++}] + (\varepsilon_{Hg^+})_{236·5} \times [Hg^+]$$

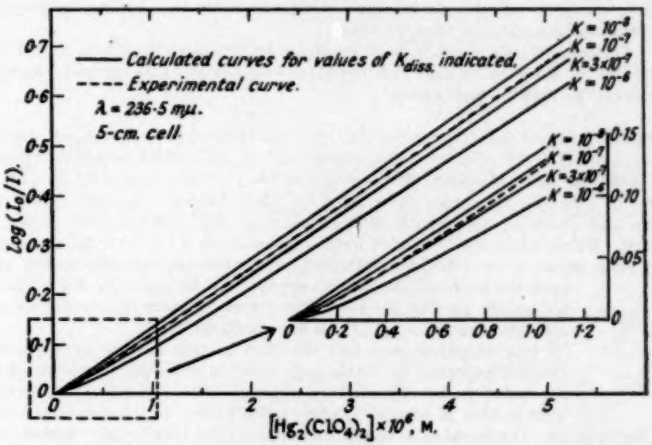
$[Hg_2^{++}]$ and $[Hg^+]$ are related to $[Hg_2(ClO_4)_2]$ through the dissociation constant $K_{diss.}$. The value of $(\varepsilon_{Hg^+})_{236·5}$ has been taken as 10^3 (Fig. 5) in all cases, log $(I_0/I)_{236·5}$ being comparatively insensitive to values of $(\varepsilon_{Hg^+})_{236·5}$ from zero to 2×10^3 except at the low concentration end of the plots, where the experimental accuracy is rather low. Appropriate values of $(\varepsilon_{Hg_2^{++}})_{236·5}$ have been calculated from the average value of $(\varepsilon_{obs.})_{236·5}$ over the range $5·10 \times 10^{-6}$—$3·0 \times 10^{-6}$M-mercurous perchlorate, the corresponding assumed value of $K_{diss.}$ being used. Fig. 6 shows the calculated curves for various $K_{diss.}$ values from 10^{-8} to 10^{-6}, and also the observed curve of optical density against total mercurous perchlorate concentration. The observed curve most nearly agrees with that calculated for $K_{diss.} = 10^{-7}$, and the general shape of the two curves is similar. The most obvious discrepancies occur at the very low concentrations, though here the values of both log $(I_0/I)_{236·5}$ and $[Hg_2(ClO_4)_2]$ were subject to greater experimental error.

It seems probable therefore that the deviations from Beer's law, which become apparent only below about 10^{-4}M-mercurous perchlorate, can be ascribed to the maintenance of the equilibrium $Hg_2^{++} \rightleftharpoons 2Hg^+$ with a value of $K_{diss.} = [Hg^+]^2/[Hg_2^{++}]$ of the order of 10^{-7} mole per litre. This value is very approximate, but $K_{diss.}$ probably lies within the limits 10^{-6} and 10^{-8}.

No experimental value for $K_{diss.}$ appears to have been reported previously, though Cartledge (*J. Amer. Chem. Soc.*, 1941, **63**, 906) has calculated ΔG for the dissociation of the dimeric ion in aqueous solution as +42 kcals. per mole, leading to a value of $K_{diss.}$ of 10^{-31}. On the other hand, Kolthoff and Barnum (*ibid.*, 1940, **62**, 3061) conclude from polarographic evidence that in concentrations of the order 10^{-20}M., mercurous mercury is almost completely in the form Hg^+. The smallest value of $K_{diss.}$ consistent with this observation is 10^{-18}.

Ogg's concentration-cell potential measurements (*Z. physikal. Chem.*, 1898, **27**, 285), although adequate to show the essentially dimeric character of mercurous mercury in concentrations

FIG. 6.



from 5×10^{-5} to 10^{-1}M., are not of sufficient accuracy to enable a calculation of $K_{diss.}$ to be made. Linhart (*J. Amer. Chem. Soc.*, 1916, **38**, 2356) has measured the potential of concentration cells of the type

$$Hg\left|\frac{x}{2}\text{M-}Hg_2(ClO_4)_2; y\text{M-}HCl\right\|y\text{M-}HCl\left|H_2; Pt—Pt; H_2\right|y\text{M-}HClO_4\left\|y\text{M-}HClO_4; x\text{M-}Hg_2(ClO_4)_2\right|Hg$$

and for values of $[Hg_2(ClO_4)_2]$ of $5{\cdot}031 \times 10^{-5}$M. and $1{\cdot}062 \times 10^{-4}$M., severally, gives a potential of 0·0089 volt, the theoretical value for a bivalent ion. The equilibrium dissociation of Hg_2^{++} at these concentrations, with a value of $K_{diss.}$ as high as 10^{-6}, would affect the observed potential by 0·3 millivolt only, of the order of the experimental error. This work does, however, establish 10^{-6} as an upper value of $K_{diss.}$. The value of pK of 7 ± 1 is thus consistent with the scanty experimental data available elsewhere, though no confirmation of this figure is forthcoming.

The use of concentration cells employing lower concentrations of mercurous perchlorate than 5×10^{-5}M. seems in principle to be the most suitable way of obtaining the dissociation constant, and it is hoped to use this method in an attempt to improve on the accuracy of the value suggested above.

The author thanks Mr. J. H. Baxendale for helpful discussion.

THE UNIVERSITY, MANCHESTER. [*Received, January 30th*, 1951.

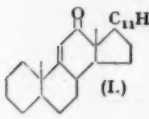
332. *Triterpenoids. Part III.* cyclo*Artenone, a Triterpenoid Ketone.*

By D. H. R. Barton.

The crystalline ketone from the fruit of *Artocarpus integrifolia* has been shown to be triterpenoid rather than steroid in character. Its formula has been established as $C_{30}H_{48}O$. By reduction with sodium and *n*-propanol the ketone has been converted into the corresponding alcohol, fully characterised by derivatives. A number of further transformation products has been prepared. The presence of an *iso*propylidene group in a side chain, and of a *cyclo*propane ring, has been demonstrated by both chemical and physical methods. The name *cyclo*artenone is proposed for the ketone, and *cyclo*artenol for the corresponding alcohol.

The non-volatile alcoholic fraction from the non-saponifiable matter of the fruit of *A. integrifolia* has been found to contain the triterpenoid alcohols *cyclo*artenol and butyrospermol.

In an extensive series of investigations Nath and his collaborators (Nath, *Z. physiol. Chem.*, 1937, **247**, 9; 1937, **249**, 71; *Science and Culture*, 1937, **3**, 297; Nath and Mukherjee, *J. Indian Chem. Soc.*, 1939, **16**, 229; Nath and Sen Gupta, *Indian J. Med. Res.*, 1939, **27**, 171; Nath and Chakraborty, *J. Indian Chem. Soc.*, 1945, **22**, 19; Nath, Chowdhury, and Uddin, *ibid.*, 1946, **23**, 245; see also Banerjee and Bhattacharyya, *Science and Culture*, 1938, **4**, 60; *Z. Krist.*, 1939, **100**, 420; Balakrishna and Seshadri, *Proc. Indian Acad. Sci.*, 1947, **26**, *A*, 46, 203; 1948, **27**, *A*, 409) have reported on a ketone contained in the non-saponifiable matter of the latex from the fruits of *Artocarpus integrifolia*. According to Nath this compound, for which he has proposed the name artostenone, is an αβ-unsaturated steroidal ketone, $C_{30}H_{50}O$, of the constitution (I).



(I.)

Our attention was first directed to this ketone by the fact that the rotation reported by Nath ($[\alpha]_D$ +24° in chloroform) was at variance with the value to be expected ($[\alpha]_D$ about +85° in $CHCl_3$).* Furthermore we were unable to accept the chemical evidence adduced by Nath as indicative of a steroid formulation. It seemed to us that artostenone might well be triterpenoid in character. The evidence reported below may be construed as confirming our criticisms of Nath's work and, for reasons that will become clear from the sequel, we have renamed the ketone cyclo*artenone*.†

A. integrifolia is common in Ceylon and we were able to obtain a supply of the latex-bearing core of the fruit through the courtesy of Dr. A. R. Lowe, Principal Research Officer of the Government Industrial Research Laboratory. The processing of this material (see Experimental) yielded crystalline *cyclo*artenone, m. p. 109°, $[\alpha]_D$ +24° (in chloroform). The physical data are in excellent agreement with those reported by Nath, but the yield of ketone was much superior (Nath, 25·6 g. from 525 fruit; this investigation, 4·95 g. from 3 fruit). Whereas Nath considered that *cyclo*artenone had the molecular formula $C_{30}H_{50}O$, all our analytical data (especially the values for hydrogen) for this compound and its derivatives indicate a $C_{30}H_{48}O$ formulation (see Table II).

Although Nath has reported degradative evidence which might be construed as proof of αβ-unsaturation in *cyclo*artenone, this is contraindicated by both physical and chemical data. *cyclo*Artenone showed $\lambda_{max.}$ 284—289 mμ. ($\varepsilon_{max.}$ 260) in the ultra-violet with no high-intensity absorption above 220 mμ. This is characteristic of a ketone grouping *isolated* from an ethylenic double bond. Furthermore, the infra-red spectrum of *cyclo*artenone (Fig. 1) showed a maximum at 5·85 μ. in carbon disulphide, a value characteristic of a *saturated* ketone grouping in a six-membered ring (compare R. Norman Jones *et al.*, *J. Amer. Chem. Soc.*, 1948, **70**, 2024). The infra-red spectrum of *cyclo*artenone showed weak absorption near 12 μ. (Fig. 1) which could be

* The rotation is calculated in the following way. All the fundamental steroid hydrocarbons have molecular rotations between 0° and +100° (Barton and Klyne, *Chem. and Ind.*, 1948, 755); changes in the saturated side chain do not cause large changes in the molecular rotation. If a mean of +50° is taken for the molecular rotation of Nath's artostane and +310° is added for the introduction of the 9(11)-en-12-one chromophore (Barton and Klyne, *loc. cit.*) the calculated molecular rotation for artostenone becomes about +360°.

† This name was kindly suggested to us by the Editor.—D.H.R.B.

interpreted (see Barton and Brooks, *J.*, 1951, 257) as indicating the grouping $-CH{=}C<$. The ultra-violet absorption spectrum, which showed $\lambda_{max.}$ 199 mμ. ($\varepsilon_{max.}$ 3,560) (see Experimental), confirmed the presence of a triply substituted ethylenic linkage.*

Reduction of *cyclo*artenone by sodium and boiling *n*-propanol afforded *cyclo*artenol, $C_{30}H_{50}O$, characterised as the acetate and benzoate. Catalytic hydrogenation of *cyclo*artenyl acetate proceeded smoothly to furnish *cyclo*artanyl acetate, hydrolysed to *cyclo*artanol, $C_{30}H_{52}O$, which was further characterised as the benzoate. The changes in molecular rotation (see

FIG. 1.

1. cyclo*Artenone* in CS_2. 2. cyclo*Artenone* in $CHCl_3$.

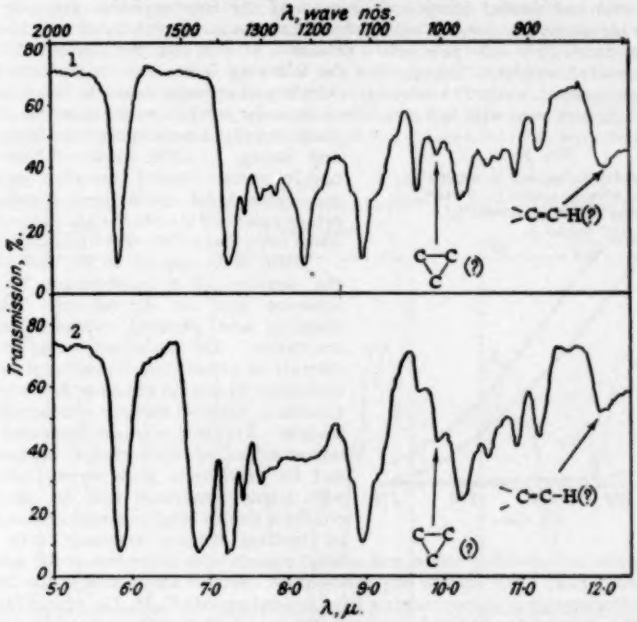


Table I) on acetylation and benzoylation of *cyclo*artenol and *cyclo*artanol are comparable with those recorded for triterpenoids rather than steroids (Barton and Jones, *J.*, 1944, 659; Barton, *J.*, 1946, 1116; Heilbron, Jones, and Robins, *J.*, 1949, 444).

The easily hydrogenated ethylenic linkage was further characterised by the preparation of *cyclo*artenyl benzoate dibromide. It was shown to be present as an *iso*propylidene grouping

TABLE I.

	$[M]_D$.				Differences.		
Compound.	Alcohol.	Acetate.	Benzoate.	Ketone.	Δ_1.	Δ_2.	Δ_3.
*cyclo*Artenol	+204°	+272°	+345°	+102°	+68°	+141°	−102°
*cyclo*Artanol	+193	+268	+351	—	+75	+158	—
α- and β-Amyrin group	—	—	—	—	+6	+145	+60
Lupeol–betulin group	—	—	—	—	+70	+200	+140
Butyrospermol	−51	+51	+180	−170	+102	+231	−119
Dihydrobutyrospermol	−60	+56	+164	−182	+116	+224	−122

* The characterisation of the degree of substitution of ethylenic linkages in the steroid and triterpenoid series by a study of their apparent absorption spectra in the 195—215-mμ. region was initiated at the University of Manchester (Bladon, Henbest, Koch, and Woods, forthcoming paper; cf. Bateman and Koch, *J.*, 1944, 600). We thank Drs. Henbest and Koch for informing us of this valuable technique before its general publication.

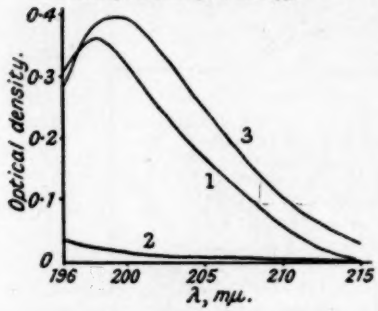
in the following way. *cyclo*Artenyl benzoate reacted smoothly with osmium tetroxide to give, after reductive fission of the osmate, dihydroxy*cyclo*artanyl benzoate, split by lead tetra-acetate into acetone and benzoyloxytrisnor*cyclo*artanal. The latter was not isolated in a state of purity but was oxidised further by silver oxide to trisnor*cyclo*artanoloic acid benzoate, characterised as the methyl ester. This ester was readily hydrolysed by boiling 1% ethanolic potassium hydroxide. The experiments prove the presence of a side chain $-CH_2\cdot CH{:}CMe_2$ and make it very probable that this can be expanded to $-CH_2\cdot CH{:}CMe_2$.

In order to facilitate comparison with other triterpenoid compounds *cyclo*artenone was reduced by the Wolff–Kishner method to the corresponding hydrocarbon *cyclo*artene, $C_{30}H_{50}$, readily hydrogenated to *cyclo*artane, $C_{30}H_{52}$.

*cyclo*Artenol and related compounds containing the *iso*propylidene grouping referred to above gave strong yellow colours with tetranitromethane. *cyclo*Artanol and its derivatives, on the other hand, gave only pale yellow colours. At first this was attributed to a strongly sterically hindered ethylenic linkage, but the following facts seem to preclude this. *cyclo*Artanyl acetate was resistant to selenium dioxide and chromic acid; it failed to react with perbenzoic acid and even with hot peracetic acid under conditions adequate for attack on the double bond of α-amyrin benzoate (Picard, Sharples, and Spring, *J.*, 1939, 1045). Whilst *cyclo*artenol and its acetate showed absorption maxima at 198 mμ., *cyclo*artanol, *cyclo*artanyl acetate, and *cyclo*artane exhibited *no selective absorption* in the ultra-violet even in the 195—210-mμ. range (see Fig. 2).

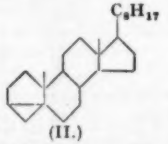
FIG. 2.

1. cyclo*Artenyl acetate* (*c*, 0·0067%).
2. cyclo*Artanyl acetate* (*c*, 0·014%).
3. *Artenyl acetate* (*c*, 0·0052%).



These facts appear to be best explained by the presence of a *cyclo*propane ring in *cyclo*artenone and its derivatives. The following chemical and physical evidence supports this conclusion. On treatment with dry hydrogen chloride in chloroform *cyclo*artanyl benzoate was isomerised to artenyl benzoate, hydrolysis of which furnished artenol further characterised as the acetate. The last was also prepared by similar isomerisation of *cyclo*artanyl acetate. Artenol and its derivatives gave strong yellow colours with tetranitromethane and the presence of an ethylenic double bond thus indicated was confirmed by treating artenyl benzoate with perbenzoic acid, to give the corresponding oxide, and artenyl acetate with perhydrol–acetic acid to furnish artenyl acetate oxide. The acetate oxide showed no selective absorption in the 280—290-mμ. region. Hydrogenation of artenyl acetate gave artanyl acetate $C_{32}H_{54}O_2$, which, like the oxides mentioned above, was saturated to tetranitromethane. This chemical evidence for the presence of a double bond in artenol was confirmed by the absorption spectra of the alcohol and its acetate: both showed maxima at 199·5 mμ. indicative of a triply substituted double bond (Fig. 2). In agreement, the infra-red absorption spectrum of the alcohol showed a weak maximum near 12 μ.

Derfer, Pickett, and Boord (*J. Amer. Chem. Soc.*, 1949, **71**, 2482) have studied the infra-red absorption spectra of a number of alkyl-substituted *cyclo*propane derivatives and have concluded that the *cyclo*propane ring is characterised by an intense band at 9·8—10·0 μ. In agreement, we find that *i*-cholestane (3 : 5-*cyclo*cholestane) (II) shows strong absorption (Fig. 3) at 9·9 μ.



(II.)

(III.)

(IV.)

The presence of a band near 10 μ. in *cyclo*artenone and *cyclo*artanyl acetate is also apparent (Figs. 1 and 4 respectively) although somewhat masked by more intense neighbouring absorption bands not present in *i*-cholestane. The assignment of this band to a *cyclo*propane ring would seem to be confirmed by the spectrum of artenol (Fig. 5), where there is no maximum

at 10 μ. The *cyclo*propane band of carane (III) and of car-3-ene (IV) is similarly flanked by neighbouring bands of greater intensity (Plíva and Herout, *Coll. Czech. Chem. Comm.*, 1950, **15**, 160).

It is of interest that even carefully purified *i*-cholestane gives a pale yellow colour with tetranitromethane and we do not believe that the weakly positive response to this test given by *cyclo*artanol derivatives can be construed as evidence against the presence of a *cyclo*propane ring. *i*-Cholestane, like the *cyclo*artanol derivatives, shows no selective absorption in the ultra-violet in the 195—210-mμ. region.

That the *cyclo*propane ring of *cyclo*artenone was not in the βγ-position with respect to the *iso*propylidene group was rendered probable by the following evidence. Treatment of *cyclo*artenyl acetate with hydrogen chloride in chloroform solution afforded artadienyl acetate hydrochloride from which artadienol, characterised as the benzoate, was obtained by alkaline hydrolysis. The crude artadienol showed no selective butadienyl absorption in the ultra-violet.

It is to be concluded that *cyclo*artenol is a new triterpenoid alcohol containing one double bond in a side chain *iso*propylidene group and five rings, one of them a *cyclo*propane ring. This is the first record of a triterpenoid compound containing the latter grouping. None of the *cyclo*artenone derivatives described in this paper appears to be identical with any other compound described in the literature.

FIG. 3.
i-Cholestane in CS_2.

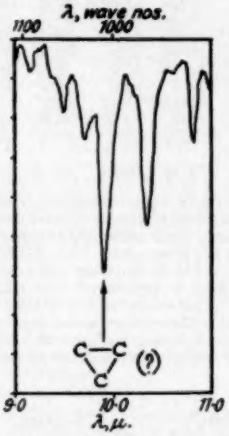


FIG. 4.
cyclo*Artanyl acetate in* CS_2.

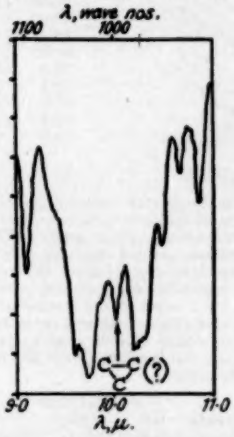
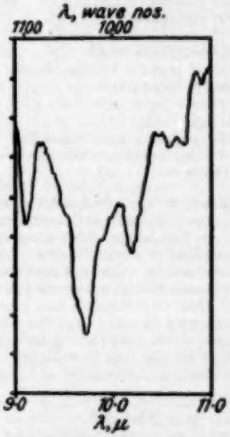


FIG. 5.
Artenol in CS_2.



It was clearly of interest to examine the non-volatile alcoholic fraction of the non-saponifiable matter, separated from *cyclo*artenone during the chromatographic fractionation of the latter. By acetylation and further chromatography the triterpenoid butyrospermyl acetate (characterised by conversion into the benzoate and the dihydro-acetate and by comparison of all three compounds with authentic specimens very kindly provided by Professor E. R. H. Jones, F.R.S., and Dr. T. G. Halsall) and *cyclo*artenyl acetate were isolated. It is possible that *cyclo*artenol and butyrospermol are related to each other, for the change in molecular rotation on oxidation of these two compounds to the corresponding ketones (Table I) is negative, an unusual feature in triterpenoid compounds (Barton and Jones, *loc. cit.*).

EXPERIMENTAL.

M. p.s are uncorrected. For rotation measurements all specimens were dried *in vacuo* at 20° below their m. p.s or at 110°, whichever was the lower temperature. All rotations were taken in chloroform solution; the values recorded have been approximated to the nearest degree. For the calculation of molecular rotations the specific rotations at $c = 2{\cdot}00$, or at the nearest concentration to this at which measurements were made, have been taken as the most suitable.

Ultra-violet absorption spectra were determined in absolute ethanol solution, using a Unicam Spectrophotometer, Model SP 500.

Unless specified to the contrary infra-red absorption spectra were determined using the Baird Associates (Cambridge, Mass.) self-recording double-beam instrument. We are indebted to Dr. Hans Heymann (Harvard) for most of the measurements recorded.

The standard chemical operations covered by the phrase, "in the usual way," were carried out as detailed in Part I of this series (Barton and Brooks, *J.*, 1951, 257).

Alkaline hydrolyses were effected by using several equivs. of potassium hydroxide and refluxing the reactants for 30—60 minutes in methanolic or dioxan–methanolic solution depending on the solubility requirements of the ester.

Light petroleum refers throughout to the fraction of b. p. 40—60°.

The analyses for new compounds, when not given in the text, are summarised in Table II.

TABLE II.

Substance.	Formula.	Found (%). C.	Found (%). H.	Reqd. (%), based on *cyclo*artenone = $C_{30}H_{48}O$, C.	Reqd. (%), based on *cyclo*artenone = $C_{30}H_{50}O$, H.	C.	H.
*cyclo*Artenone	$C_{30}H_{48}O$	84·8	11·3	84·85	11·4	84·45	11·8
*cyclo*Artenol	$C_{30}H_{50}O,\frac{1}{2}CH_3{\cdot}OH$	82·4	11·8	82·75	11·85	82·35	12·25
*cyclo*Artenyl acetate	$C_{32}H_{52}O_2$	82·15	11·1	82·0	11·2	81·65	11·55
*cyclo*Artenyl benzoate	$C_{37}H_{54}O_2$	83·25	10·15	83·7	10·2	83·4	10·6
*cyclo*Artenyl benzoate dibromide	$C_{37}H_{54}O_2Br_2$	64·7	7·8	64·35	7·85	64·15	8·15
*cyclo*Artanol	$C_{30}H_{52}O,\frac{1}{2}CH_3{\cdot}OH$	82·1	12·3	82·35	12·25	82·0	12·65
*cyclo*Artanyl acetate	$C_{32}H_{54}O_2$	81·5	11·45	81·65	11·55	81·3	11·9
*cyclo*Artanyl benzoate	$C_{37}H_{56}O_2$	83·2	10·6	83·4	10·6	83·1	10·95
Artenol	$C_{30}H_{52}O$	83·75	12·0	84·05	12·25	83·6	12·65
Artenyl acetate	$C_{32}H_{54}O_2$	81·85	11·7	81·65	11·55	81·3	11·9
Artanyl acetate	$C_{32}H_{56}O_2$	80·95	11·95	81·25	11·95	80·9	12·35
Artenyl benzoate	$C_{37}H_{56}O_2$	82·95	10·2	83·4	10·6	83·1	10·95
Artenyl acetate oxide	$C_{32}H_{54}O_3$	78·7	11·05	78·95	11·2	78·6	11·55
Artenyl benzoate oxide	$C_{37}H_{56}O_3$	80·55	10·4	80·95	10·3	80·65	10·65
Artadienyl acetate hydrochloride	$C_{32}H_{53}O_2Cl$	76·6	10·6	76·05	10·6	75·75	10·9
Artadienyl benzoate	$C_{37}H_{54}O_2$	83·2	10·15	83·7	10·2	83·4	10·6
*cyclo*Artene	$C_{30}H_{50}$	87·9	12·05	87·75	12·25	87·3	12·65
*cyclo*Artane	$C_{30}H_{52}$	87·5	12·45	87·3	12·65	86·9	13·15
Dihydroxy*cyclo*artanyl benzoate	$C_{37}H_{56}O_4$	78·8	9·9	78·65	10·0	78·4	10·35
Methyl trisnor*cyclo*artanoloate benzoate	$C_{35}H_{50}O_4$	78·3	9·05	78·55	9·45	78·25	9·8

Extraction of cyclo*Artenone from the Fruit of* A. integrifolia.—The inner, latex-containing cores of three large ripe fruit had been sealed, with addition of some chloroform, in tinned cans. The following procedure was adopted for the extraction of the *cyclo*artenone. The cores were milled thoroughly in a Waring Blender with addition of chloroform, and the resulting pulp was left overnight. The chloroform was removed by filtration and the pulp washed with more chloroform. The chloroform was removed *in vacuo* and the gummy residue was saponified by refluxing it with 25 g. of potassium hydroxide in 250 ml. each of methanol and benzene for 2 hours on the steam-bath. The benzene and methanol were then removed *in vacuo* and the non-saponifiable matter was extracted from the residue in the usual way. This procedure furnished a brown gum, which was chromatographed over a large column of alumina (Merck) with the results indicated below. All fractions, were 200 ml. in volume and, after evaporation, were set side for one month at room temperature.

Fraction no.	Eluent.*	Eluate.	Fraction no.	Eluent.*	Eluate.
1—2	1 : 1 Pet.-C_6H_6	Gum	11	C_6H_6	Gum
3—4	,, ,,	Cryst. (large fractions)	12	9 : 1 C_6H_6–Et_2O	Gum
5—7	,, ,,	Cryst.	13	4 : 1 ,,	Gum
8	,, ,,	Cryst. (small fraction)	14	1 : 1 ,,	Gum (small fraction)
9—10	C_6H_6	Partly cryst.	15	1 : 1 Et_2O–MeOH	Partly cryst. (small fraction)

* Pet. = light petroleum.

Fractions 3—8 were combined and rechromatographed in the same way. The results are indicated below.

Fraction no.	Eluent.	Eluate.
16	200 ml. Pet.	Gum (small fraction)
17	200 ml. ,,	Gum, cryst. on storage
18—22	200 ml. ,,	All small cryst. fractions
23—24	400 ml. 1 : 9 C_6H_6–Pet.	Larger cryst. fractions
25—26	400 ml. 1 : 4 ,,	Large cryst. fractions
27	400 ml. 1 : 1 ,,	Small fraction : cryst.
28	400 ml. C_6H_6	Trace, not cryst.
29	400 ml. 1 : 19 Et_2O–C_6H_6	Small fraction; slowly cryst.
30—31	400 ml. 1 : 9 ,,	Larger fractions; slowly cryst.
32	400 ml. 1 : 1 Et_2O–MeOH	Viscous gum

Fractions 18—24 were recrystallised once from benzene–methanol to give 2·65 g. of pure *cyclo*artenone, m. p. 109°, $[\alpha]_D$ +24° (*c*, 3·39), $[M]_D$ +102°, $\lambda_{max.}$ 199 mμ., $\varepsilon_{max.} = 3560$, $\varepsilon_{315} = 780$.

(*c*, 0·004), $\lambda_{max.}$ 284—289 mμ., $\varepsilon_{max.}$ = 260. Fractions 23 and 24, combined and recrystallised once from benzene–methanol, gave 2·3 g. of *cyclo*artenone, m. p. 105°. Pure *cyclo*artenone showed a yellow colour, changing through orange with a green fluorescence to red, in the Liebermann–Burchard reaction. It gave a yellow colour with tetranitromethane.

Fractions 17 and 27 were combined and converted into crude *cyclo*artenyl acetate (see below). Subsequent recrystallisation of the crude acetate furnished 0·6 g. of pure acetate.

Fractions 11—14 were combined with fractions 29—32 and worked up further as detailed below.

cyclo*Artenol.*—*cyclo*Artenone (1·6 g.) in *n*-propyl alcohol (100 ml.) was treated with sodium under reflux until saturated. The reaction mixture was diluted with water and extracted with ether. Evaporation of the ether and addition of methanol furnished cyclo*artenol*, recrystallised from chloroform–methanol in clumps of needles, m. p. 85—92° (decomp.) after sintering at 80°, $[\alpha]_D$ +48° (*c*, 5·03), $[M]_D$ +204°, $\lambda_{max.}$ 198 mμ., $\varepsilon_{max.}$ = 3,200 (*c*, 0·0094). It was not possible to raise the m. p. of *cyclo*artenol to that (106—107°) recorded by Nath (*Z. physiol. Chem.*, 1937, **247**, 17) for a (not analysed) specimen of the same compound.

cyclo*Artenyl Acetate.*—This was prepared by acetylation of *cyclo*artenol in pyridine with acetic anhydride at room temperature (24 hours) or at steam-bath temp. (30 minutes). The *acetate*, worked up in the usual way and recrystallised from chloroform–methanol in small plates, had m. p. 122·5—123·5°, $[\alpha]_D$ +58° (*c*, 5·34), $[M]_D$ +272°, $\lambda_{max.}$ 198 mμ., $\varepsilon_{max.}$ = 2,540, ε_{215} = 700 (*c*, 0·0067).

cyclo*Artenyl Benzoate.*—*cyclo*Artenol, in pyridine solution, was treated with benzoyl chloride at room temperature for 48 hours. The reaction mixture was worked up in the usual way. Crystallisation from chloroform–methanol furnished cyclo*artenyl benzoate* in long needles, m. p. 129—130°, $[\alpha]_D$ +65° (*c*, 5·50), $[M]_D$ +345°.

cyclo*Artenyl Benzoate Dibromide.*—*cyclo*Artenol benzoate in chloroform solution was treated at room temperature with a dilute solution of bromine in the same solvent until bromine was no longer absorbed. Washing with aqueous sodium hydrogen carbonate, evaporation *in vacuo*, and recrystallisation of the residue from chloroform–methanol afforded cyclo*artenyl benzoate dibromide*, m. p. 182—183° (decomp.) (taken rapidly) (Found: Br, 24·1. $C_{37}H_{54}O_2Br_2$ requires Br, 23·2%). With tetranitromethane the dibromide gave a pale yellow colour.

cyclo*Artanyl Acetate.*—*cyclo*Artenyl acetate (500 mg.) in glacial acetic acid (100 ml.) was hydrogenated using a platinum catalyst for 2 hours. Working up in the usual way and recrystallisation from chloroform–methanol afforded beautiful long needles of cyclo*artanyl acetate*, m. p. 132—133°, $[\alpha]_D$ +57° (*c*, 5·31), $[M]_D$ +268°, which had no selective absorption in the 195—300-mμ. range. The acetate gave a pale yellow colour with tetranitromethane. It was recovered unchanged in almost quantitative yield (*a*) on treatment with a ten-fold excess of perbenzoic acid at 5° for 15 days, (*b*) on treatment with perhydrol–acetic acid on the steam-bath according to the directions of Picard, Sharples, and Spring (*J.*, 1939, 1045) for α-amyrin benzoate, and (*c*) on refluxing with selenium dioxide (½ its wt.) in acetic acid for 12 hours. On chromic acid oxidation (½ its wt. of CrO_3) in acetic acid, at temperatures from 70° to 90° and reaction times from 0·5 to 1·5 hours *cyclo*artanyl acetate was, for the main part, recovered unchanged. In each experiment chromatographic fractionation was carried out but, apart from unchanged starting material, the reaction products were gummy and intractable. There was no indication of the formation of a yellow ene-1 : 4-dione, such as results from the oxidation of dihydrolanosteryl acetate or dihydroeuphyl acetate.

cyclo*Artanol.*—Alkaline hydrolysis of *cyclo*artanyl acetate in the usual way afforded cyclo*artanol*, recrystallised from aqueous methanol, m. p. 99—101° (decomp.), $[\alpha]_D$ +45° (*c*, 3·59), $[M]_D$ +193°, which had no selective absorption in the ultra-violet. *cyclo*Artanol gave a pale yellow colour with tetranitromethane.

Benzoate. *cyclo*Artanol was treated as for *cyclo*artenol (see above) to give the benzoate which, recrystallised from chloroform–methanol, had m. p. 137—138° to a cloudy melt clearing sharply at 148—149°, $[\alpha]_D$ +66° (*c*, 4·62), $[M]_D$ +351°. There was a beautiful and intense play of colours from the m. p. to the clearing point. *cyclo*Artanyl benzoate gave a pale yellow colour with tetranitromethane.

Artenyl Benzoate.—*cyclo*Artanyl benzoate (200 mg.) in dry chloroform (20 ml.) was treated at room temperature with a vigorous stream of hydrogen chloride for 30 minutes. The chloroform was removed *in vacuo* and the residue recrystallised from chloroform–methanol to furnish *artenyl benzoate*, m. p. 197—198°, $[\alpha]_D$ +78° (*c*, 3·05). Treatment of 200 mg. of this benzoate (2nd crop) with twice the theoretical amount of perbenzoic acid in chloroform solution at 0° for 2 days gave *artenyl benzoate oxide*; recrystallised from chloroform–methanol, this had m. p. 205—208° (decomp.), $[\alpha]_D$ +54° (*c*, 1·79). The former benzoate gave a strong yellow colour with tetranitromethane, but with the latter the test was negative.

Artenol.—Alkaline hydrolysis of artenyl benzoate afforded *artenol*; recrystallised from chloroform–methanol, this had m. p. 152—154°, $[\alpha]_D$ +57° (*c*, 1·61), $\lambda_{max.}$ 199·5 mμ., $\varepsilon_{max.}$ = 4000, ε_{215} = 760 (*c*, 0·0082).

Acetate. (*a*) Artenol was acetylated with acetic anhydride in pyridine solution at room temperature overnight. Working up in the usual way and recrystallisation from chloroform–methanol gave the acetate in needles, m. p. 165—167°.

(*b*) *cyclo*Artanyl acetate (250 mg.) in dry chloroform (20 ml.) was treated with a vigorous stream of hydrogen chloride for 45 minutes. The chloroform was removed *in vacuo* and the residue recrystallised to give the same acetate, m. p. 165—167°, $[\alpha]_D$ +73° (*c*, 1·34), $\lambda_{max.}$ 199·5 mμ., $\varepsilon_{max.}$ = 3600, ε_{215} = 300 (*c*, 0·0052). Both artenol and its acetate gave strong yellow colours with tetranitromethane.

It was noted that, whilst artenol and its benzoate appeared to be homogeneous on crystallisation, acetylation of the alcohol gave an acetate which was purified only by repeated recrystallisation. It is possible therefore that artenol and its benzoate are contaminated with minor amounts of double-bond isomers not readily separable by crystallisation. Lack of material prevented a more extensive investigation of this phenomenon.

Treatment of artenyl acetate (2nd crop) with perhydrol–acetic acid on the steam-bath as in the procedure of Picard, Sharples, and Spring (*loc. cit.*) furnished *artenyl acetate oxide*; recrystallised from chloroform–methanol, this melted at 184—185°. It showed no selective absorption in the ultra-violet and gave no indication of a carbonyl band in the 280—290-mμ. region. The tetranitromethane test was negative.

Artanyl Acetate.—Artenyl acetate (10 mg.) in AnalaR acetic acid (20 ml.) and dry ether (10 ml.) was hydrogenated using a platinum catalyst (200 mg.) for 4 hours. Working up in the usual way afforded *artanyl acetate*, which recrystallised from methanol as matted needles, m. p. 148—149° (tetranitromethane test negative).

cyclo*Artene.*—*cyclo*Artenone (200 mg.) in anhydrous hydrazine (2 ml.) and absolute alcohol (6 ml.) containing dissolved sodium (250 mg.) was heated at 180° for 18 hours. Working up in the usual way and chromatography over alumina (Savory and Moore's standardised) afforded cyclo*artene*; recrystallised from methanol, this had m. p. 49—50° and $[\alpha]_D$ +59° (*c*, 0·88).

cyclo*Artane.*—*cyclo*Artene (30 mg.) in AnalaR acetic acid (20 ml.) and anhydrous ether (10 ml.) was hydrogenated using a platinum catalyst (100 mg.) for 2 hours. Working up in the usual way furnished cyclo*artane*; recrystallised from chloroform–methanol, this had m. p. 85—86° and $[\alpha]_D$ +59° (*c*, 1·48), but no selective absorption in the ultra-violet *cyclo*Artane gave a pale yellow colour with tetranitromethane.

Artadienyl Acetate Hydrochloride.—*cyclo*Artenyl acetate (200 mg.) in chloroform (25 ml.) was treated with gaseous hydrogen chloride at room temperature for 30 minutes. Removal of the solvent *in vacuo* and recrystallisation of the residue from chloroform–methanol gave *artadienyl acetate hydrochloride*, m. p. 170—172°, $[\alpha]_D$ +64° (*c*, 1·04).

This hydrochloride (100 mg.) was refluxed with excess of methanolic potassium hydroxide for 2·5 hours and the reaction product worked up in the usual way. Benzoylation (pyridine solution on the steam-bath for 30 minutes) and chromatography over alumina (Savory and Moore's standardised) gave *artadienyl benzoate* which, recrystallised from chloroform–methanol, had m. p. 185—187° and $[\alpha]_D$ +80° (*c*, 1·41).

Action of Osmium Tetroxide on cyclo*Artenyl Benzoate.*—*cyclo*Artenyl benzoate (610 mg.) in anhydrous ether (100 ml.) was treated with osmium tetroxide (900 mg.) dissolved in the same solvent (50 ml.) and kept for 5 days at room temperature. The ether was removed *in vacuo*, sodium sulphite (23 g.) in water (230 ml.) and ethanol (115 ml.) were added, and the whole was refluxed for 2 hours. The mixture was filtered hot and the filtrate diluted with water and extracted with ether. Evaporation of the ether afforded a solid which was purified by chromatography over alumina (Savory and Moore). Methanol–ether (1 : 19) eluted *dihydroxy*cyclo*artanyl benzoate*, which recrystallised from methanol as fine plates, m. p. 180—183° (decomp.), $[\alpha]_D$ +66° (*c*, 1·18). It gave a pale yellow colour with tetranitromethane.

Dihydroxy*cyclo*artanyl benzoate (200 mg.) in AnalaR acetic acid (25 ml.) was treated with lead tetra-acetate (250 mg.) in the same solvent (25 ml.) at room temperature for 5 hours. The mixture was diluted with water (30 ml.) and distilled to half the volume. Treatment of the distillate in the usual way with 2 : 4-dinitrophenylhydrazine hydrochloride gave a yellow precipitate. After chromatography in benzene solution over alumina (Savory and Moore) this furnished acetone 2 : 4-dinitrophenylhydrazone (30 mg.); recrystallised from aqueous methanol, this had m. p. 125—126°, undepressed on admixture with an authentic specimen of the same m. p. (Found: C, 45·65; H, 4·2. Calc. for $C_9H_{10}O_4N_4$: C, 45·35; H, 4·25%).

The non-volatile products of the lead tetra-acetate oxidation crystallised as needles from the acetic acid mother-liquors on storage. Addition of water and ether, filtration, separation of the ethereal layer, and working up in the usual way afforded an acid fraction (insoluble potassium salt) and a larger neutral fraction. The latter was oxidised by silver oxide (Kuhn, Badstübner, and Grundmann, *Ber.*, 1936, **69**, 106), and the resulting acid fraction added to the first acid fraction. The combined acid fractions were methylated with diazomethane, and the resulting methyl ester was chromatographed over alumina (Savory and Moore). Elution with benzene afforded *methyl trisnor*cyclo*artanoloate benzoate* which, recrystallised from aqueous methanol, had m. p. 133—134°, $[\alpha]_D$ +65° (*c*, 1·47). The ester gave a pale yellow colour with tetranitromethane.

Methyl trisnor*cyclo*artanoloate benzoate (50 mg.) was refluxed with 1% absolute ethanolic potassium hydroxide (50 ml.) for 2 hours. The alcohol was removed *in vacuo*; the residue contained no neutral fraction.

Examination of the Alcohol Fraction from the Fruit of A. integrifolia.—Fractions 11—14 combined with fractions 29—32 of the chromatograms (see p. 1448) represented the alcohol fractions from the extract of *A. integrifolia*. They were combined and acetylated with pyridine–acetic anhydride on the water-bath for 1 hour. Working up in the usual way gave a very viscous mixture of acetates which did not solidify. The mixture was chromatographed over 400 g. of Savory and Moore alumina with the following results (each fraction crystallised once from chloroform–methanol before the m. p. was taken).

Fraction no.	Eluent.	Eluate.
1—4	400 ml. 9 : 1 Pet.–C_6H_6	Nothing
5	100 ml. 4 : 1 ,,	Solid; m. p. 96—100°
6	,, ,,	Solid, m. p. 116—123°
7	,, ,,	Solid, m. p. 134—136°
8	100 ml. 3 : 1 ,,	Cryst. easily, m. p. 112—115°
9	200 ml. 3 : 1 ,,	Cryst. very easily, m. p. 118—120°
10	,, ,,	Cryst. very easily; m. p. 118—120°
11	200 ml. 1 : 1 ,,	Cryst. very easily, m. p. 118—120°
12	200 ml. C_6H_6	Small amorphous fraction
13—16	800 ml. ,,	Traces only; oily

Recrystallisation of fraction 8 gave plates, m. p. 121—123°. These were combined with fractions 9, 10, and 11 (total wt. 1·35 g.) and recrystallised once from chloroform–methanol to give *cyclo*artenyl acetate, m. p. 122—123°, undepressed on admixture with the acetate (see above) obtained from *cyclo*artenone, $[\alpha]_D$ +58° (*c*, 3·00).

Recrystallised fraction 6 had m. p. 133—135°. It was combined with fraction 7 (total wt. 350 mg.) and recrystallised three times from chloroform–methanol, giving needles, m. p. 141—143°, $[\alpha]_D$ +14° (*c*, 3·21) (Found: C, 82·0; H, 11·35. Calc. for $C_{32}H_{52}O_2$: C, 82·0; H, 11·2%). There was no depression in m. p. on admixture with an authentic specimen of butyrospermyl acetate, m. p. 141—143°. Hydrogenation over a platinum catalyst in ether–acetic acid solution furnished a dihydro-acetate which, recrystallised from methanol, had m. p. 132—133° (Found: C, 81·8; H, 11·45. Calc. for $C_{32}H_{54}O_2$: C, 81·65; H, 11·55%). There was no depression in m. p. on admixture with an authentic specimen of dihydrobutyrospermyl acetate, m. p. 133—134°. Alkaline hydrolysis of the acetate isolated from *A. integrifolia* and benzoylation (pyridine–benzoyl chloride overnight) afforded the corresponding benzoate (from methanol), m. p. 128—130°, $[\alpha]_D$ +33° (*c*, 1·45), undepressed on admixture with an authentic specimen of dihydrobutyrospermyl benzoate, m. p. 130—132°.

i-Cholestane.—A reference specimen of this hydrocarbon was prepared from *i*-cholestenone by Schmid and Kägi's method (*Helv. Chim. Acta*, 1950, **33**, 1582). In spite of careful chromatographic fractionation and repeated recrystallisation from chloroform–methanol it always melted at 80—81°, had $[\alpha]_D$ +80° (*c*, 2·81), showed no selective absorption from 195 to 220 mμ. (*c*, 0·0113%), and gave a pale yellow colour with tetranitromethane of an intensity corresponding to that given by *cyclo*artanol and its derivatives retaining the unopened *cyclo*propane ring.

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333. *The Enzymic Synthesis and Degradation of Starch. Part XIV. R-Enzyme.*

By P. N. HOBSON, W. J. WHELAN, and STANLEY PEAT.

An enzyme (R-enzyme), which catalyses the scission of branch links in amylopectin, has been isolated from the potato and the broad bean as a stable amorphous powder.

It is shown that R-enzyme operates by a purely hydrolytic process and that, unlike Q-enzyme, it has no link-synthesising function. It is a "debranching" enzyme with respect to the predominant type of branch linkage in amylopectin, the 1 : 6-glucosidic link. It neither makes nor breaks chain-forming 1 : 4-links and has no action on amylose (synthetic or natural) or on the linear dextrins related to amylose.

A convenient method of estimating the activity of R-enzyme is based on the fact that its action on amylopectin or limit β-dextrin is accompanied by a *rise* in the iodine-staining power of the substrate.

IT has been shown in Part VII of this series (*J.*, 1950, 93) that, if the conversion of amylose into amylopectin by the agency of Q-enzyme is a reversible reaction, then at equilibrium the unbranched component must be present in a negligible proportion; in a practical sense, Q-enzyme action is irreversible. As reported in a preliminary notice (*Biochem. J.*, 1950, **47**, xxxix) we have been able to isolate from both the potato and the broad bean an enzyme (R-enzyme) which, in part, reverses the reactions catalysed by Q-enzyme. R-Enzyme is a "debranching" enzyme inasmuch as it effects the scission of the branch links in amylopectin. This appears to be a purely hydrolytic process and R-enzyme, unlike Q-enzyme, shows no synthetic activity.

R-Enzyme was first encountered during exploration of methods for the removal of the traces of α-amylolytic activity which persisted in the purest Q-enzyme preparations (see Part VII, *loc. cit.*). During this study an attempt was made, following Holmberg (*Biochem. Z.*, 1933, **258**, 134), preferentially to adsorb the α-amylase impurity on starch grains. The Q-enzyme of broad bean was isolated at the Q1-stage by the method described in Part X (*J.*, 1950, 3566) and a solution of this Q-preparation in 20% ethanol was stirred at 0° with potato starch. When treated in this way, the Q-preparation lost its α-amylolytic activity but, what was more

unexpected, its Q-enzyme activity also disappeared. Nevertheless the starch-treated solution (which was without action on amylose) contained an enzyme, which was characterised by the fact that it caused an *increase* in the blue values of limit β-dextrin (Table I) and amylopectin (Table III). This enzyme we describe, noncommittally, as R-enzyme. In our earlier work, a transitory rise in the blue value of a β-dextrin digest with Q-enzyme was occasionally observed and, after the discovery of R-enzyme, we were able to demonstrate that a Q3-preparation did contain the new enzyme. When β-dextrin was incubated with a bean Q-enzyme at an acid pH (5·2), the activity of any α-amylase was suppressed, and a definite increase in blue value was observed (Table XII).

R-Enzyme was isolated as a stable powder, the activity of which was quoted in terms of the time taken to increase the blue value of β-dextrin from 0·15 to 0·20, under standardised conditions. Its pH and temperature optima were found to be 6·5—7·0 and *ca.* 34° respectively. R-Enzyme is not a phosphorylase and its action on β-dextrin is not influenced by added phosphate (Table II) although most preparations contain traces of phosphorylase (*e.g.*, 1 unit in 430 mg.).

The data in Table III show that the increase in blue value of amylopectin (and of branched dextrins derived from it) effected by R-enzyme is coincident with an increase in the extent of conversion into maltose by β-amylase. For example, the action of R-enzyme on β-dextrin occasions a rise in the blue value from 0·145 to a constant value of 0·265 and at the same time the β-amylolysis limit increases from 2·8 to 61·6% conversion. Clearly the β-dextrin is much less highly branched (and therefore more susceptible to hydrolysis by β-amylase) after it has been acted upon by R-enzyme. This effect can only be due to the scission of the branch links in the β-dextrin and, since a large majority of these are hydrolysed by R-enzyme (Table III), it follows that they must be of the predominant 1 : 6-glucosidic type.

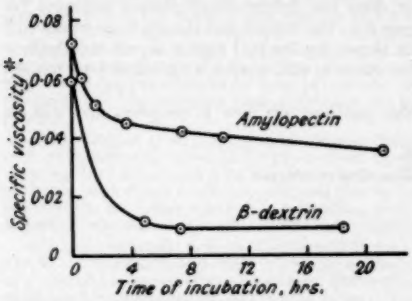
Only branched polysaccharides of the amylopectin type function as substrates for R-enzyme. Its action on an amylose of high blue value is negligible and, as can be calculated from the data in Table III, its activity with respect to whole starch or an imperfectly separated amylose is proportional to their amylopectin content. It is evident that R-enzyme, unlike Q-enzyme or the amylases, is incapable of hydrolysing 1 : 4-glucosidic chain links.

At first sight, the fact that R-enzyme effects an increase in the blue values of branched polysaccharides might be regarded as an indication of a synthetic function involving increases in chain length. If this were so, R-enzyme by cleaving 1 : 6-links and synthesising chain-forming 1 : 4-links would be exactly reversing Q-enzyme action, which is thermodynamically impossible unless a different mechanism is involved in the reversal. There is ample evidence, however, that R-enzyme does not catalyse the conversion of amylopectin into amylose, *i.e.*, reverse Q-enzyme action. (1) Although R-enzyme increases the blue value of amylopectin, the maximum blue value attained (0·25) never approaches that of amylose (1·4). (2) The conversion limit (with a stock β-amylase preparation) of the product (dextrin-R) of the action of R-enzyme on amylopectin is 66% (see Table III) whereas that of amylose is >90%. (3) Dextrin-R does not function as a substrate for the introduction of branches by Q-enzyme as is demonstrated by the negligible difference in the limits of β-amylolysis before and after Q-enzyme action (Table XI). It would seem that the linear chains (*ca.* 20 glucose units) derived from amylopectin by the debranching action of R-enzyme are too short to function as substrate for Q-enzyme (cf. Part XII, *J.*, 1951, 596). Analogous observations were made on a β-dextrin treated with R-enzyme (Table X). (4) A quantitative estimation showed that the phosphorylase-priming activity of amylopectin was essentially unchanged by treatment with R-enzyme (Table V). The priming activity of the amylopectin would have been lower if the proportion of *non-reducing* chain ends had been diminished by the synthesis of 1 : 4-links by R-enzyme. (5) A complete reversal of Q-enzyme action implies that R-enzyme effects the synthesis of a 1 : 4-link for every 1 : 6-link severed. If this were so, the proportion of *reducing* chain-ends in amylopectin or β-dextrin would remain unaltered. Actually the copper-reducing power of β-dextrin increased from 0 to 11·4% under the action of R-enzyme although the observed increase with amylopectin was much smaller (Table IV). (6) Similarly, if R-enzyme exchanges 1 : 4- for 1 : 6-linkages, then dextrin-R would have the same molecular weight as the amylopectin from which it was derived, but its structure would be more linear. It is to be expected therefore that, in solution, dextrin-R would show either the same, or a greater, viscosity, but Fig. 1 reveals that the relative viscosity of amylopectin is halved by R-enzyme action. The effect on the viscosity of β-dextrin is even more marked (85% fall). It is evident that R-enzyme does not catalyse the conversion of amylopectin into amylose and that it does not increase the length of the linear repeating chains of either amylopectin or β-dextrin. It is reasonable to conclude therefore that R-enzyme neither makes nor breaks 1 : 4-linkages.

It is important to note the bearing of this conclusion on the problem of the rise of blue value observed when R-enzyme acts on a branched amylaceous polysaccharide. Since R-enzyme does not synthesise 1 : 4-linkages, it follows that the rise in blue value is directly associated with the scission of branch linkages. In other words, the blue value of a polysaccharide composed of unbranched chains is higher than that of a structure in which chains of the same average length are mutually combined by branch links.

FIG. 1.

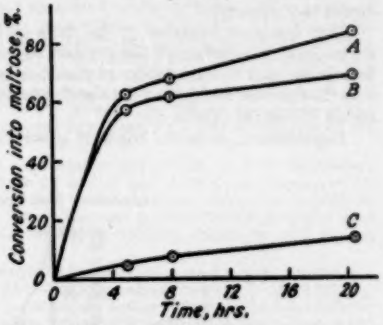
Action of R-enzyme on amylopectin and β-dextrin. Viscosity changes.



* *Relative to control digest without polysaccharide.*

FIG. 2.

Simultaneous action of β-amylase and R-enzyme on β-dextrin.



A.—β-Amylase + R-enzyme.
B.—β-Amylase + R-enzyme, corrected for action of β-amylase alone.
C.—β-Amylase alone.

It remains to be decided whether R-enzyme catalyses a reversible reaction, *i.e.*, the synthesis as well as the scission of branch 1 : 6-linkages. It will be recalled (Table III) that only about two-thirds of the branch links in amylopectin (and slightly fewer in β-dextrin) are severed by R-enzyme. This could be caused by the establishment of an equilibrium between branched and unbranched structures of the same basal chain-length, thus

On such a view, the addition of β-amylase to the equilibrium mixture *after* the destruction of the R-enzyme by heat would result in the complete hydrolysis of the unbranched and the partial hydrolysis of the branched chains. If, however, the β-amylase were added while the R-enzyme were still present and active, the disturbance of the equilibrium, consequent upon the hydrolysis of the linear chains by the β-amylase, would result in the further debranching of the ramified structures by R-enzyme. Ultimately the whole of the β-dextrin would be converted into maltose. But this does not happen. The simultaneous action of R-enzyme and β-amylase on limit β-dextrin results in a conversion into maltose of about 60% only (Fig. 2), a limit which is essentially the same as that recorded for the successive actions of R-enzyme and β-amylase on the dextrin (Table III).

Another line of attack provided further evidence that R-enzyme is incapable of synthesising 1 : 6-linkages. A series of α-dextrins was prepared from amylose by the agency of α-amylase. These dextrins which consisted essentially of unbranched chains of widely varying lengths were submitted to the action of R-enzyme for 19 hours. Thereafter the enzyme was killed and the limit of hydrolysis of the product by β-amylase determined. Two α-dextrins, one of relatively high and one of low blue value, were used and in each case no significant difference in the degree of β-amylolysis was observed between the R-enzyme-treated dextrin and the original α-dextrin (Table VIII). In other words, R-enzyme had not effected the cross-linking of any of these linear α-dextrins. The confirmatory observation was also made that R-enzyme does not influence the shape of the curve, % fall of amylose value–% conversion into maltose, obtained

when amylose is submitted to α-amylolysis. The curves for α-amylase alone and for α-amylase and R-enzyme acting together were identical (Fig. 3).

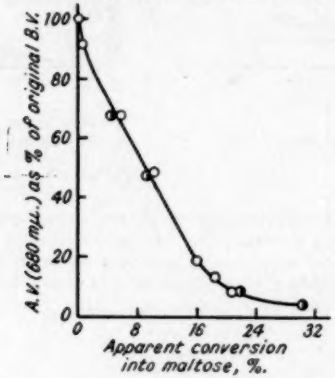
Further support came from a study of the effect of R-enzyme on the synthesis of polysaccharide from glucose-1 phosphate by the agency of phosphorylase. The development of iodine-staining power was followed quantitatively in two digests, one containing potato phosphorylase, glucose-1 phosphate, and an achroic primer, and the other containing R-enzyme in addition. The results given in Table IX show that in each case the rates of synthesis are the same and the products have practically the same blue values. Substrates with chain-lengths up to that of amylose were thus presented to R-enzyme and had it been capable of synthesising 1 : 6-linkages, a ramified structure of lower blue value would have been formed in the second digest (see above).

One question remains to be answered. Why does the debranching process initiated by R-enzyme cease before all the barriers to β-amylolysis (*i.e.*, the branch links) have been removed? This is not due to exhaustion of the R-enzyme as is shown by the fact that a digest of β-dextrin with R-enzyme which has attained maximum blue value is still active with respect to freshly added β-dextrin (Table I).

Experiments directed towards a solution of this problem are now in progress and will be

FIG. 3.

Action of R-enzyme and α-amylase on amylose.



○ *α-Amylase alone.* ◑ *R-enzyme + α-amylase.*

reported in a later communication together with an account of the isolation and the properties of the products of the action of R-enzyme on amylopectin and limit β-dextrin.

Hints have not been lacking in the recent literature of the existence of one or more polysaccharide-debranching enzymes in both plant and animal cells. K. H. Meyer and Bernfeld (*Helv. Chim. Acta*, 1942, **25**, 399) demonstrated the presence of an enzyme in yeast which degraded β-dextrin. This was regarded as a phosphorolysing enzyme. It was claimed by Petrova (*Biokhimiya*, 1948, **13**, 244; 1949, **14**, 155) that muscle contains an "amylose isomerase" which synthesises and hydrolyses polysaccharides with 1 : 6-linkages. This enzyme is probably akin to the "amylo-1 : 6-glucosidase" found in muscle by Cori and Larner (*Fed. Proc.*, 1950, **9**, No. 1). Knee and Spoerl (*Chem. Abs.*, 1949, **43**, 8407) make reference to a "limit dextrinase" which is associated with the amylases of malt in the conversion of starch into fermentable sugar. Tsuchiya, Montgomery, and Corman (*J. Amer. Chem. Soc.*, 1949, **71**, 3265) report the presence in the culture filtrate of *Aspergillus niger* of an enzyme capable of hydrolysing the α-1 : 6-glucosidic link in *iso*maltose. Maruo and Kobayashi (*J. Agr. Chem. Soc.*, 1949, **23**, 115) conclude that Nishimura's "amylosynthease" from autolysed yeast is a debranching enzyme in that it converts glutinous-rice starch into a product which is considered to have long glucose chains with fewer branching points. It is proposed by these authors (*Nature*, 1951, **167**, 606) to change the name "amylosynthease" to "iso-amylase." Finally should be mentioned the discovery of a mould dextranase which is capable of hydrolysing with equal ease almost all the 1 : 6-links in dextran (Hultin and Nortström, *Acta Chem. Scand.*, 1949, **3**, 1405) and the

" maltase " isolated from *Clostridium acetobutylicum* by French and Knapp (*J. Biol. Chem.*, 1950, **187**, 463). This maltase hydrolyses the branch links and the chain links of starch as well as the 1 : 4-linkage in maltose.

Experimental.

Analytical Methods.—For the methods used in measurement of the iodine-stains of polysaccharides, inorganic and ester phosphorus, and phosphorylase activity see Part IV of this series (*J.*, 1949, 1705). The methods of determining reducing power and β-amylase activity and of preparing starch fractions and limit β-dextrin (dextrin-A) are given in Part X (*J.*, 1950, 3566).

Preparation of R-Enzyme.—A Q1-precipitate was prepared from " Prolific Longpod " broad-bean flour (300 g.) as described in Part X. The precipitate was dissolved in ice-cold water (100 c.c.), then centrifuged to remove a little gummy residue, and to the supernatant liquid anhydrous sodium sulphate (1·0 g.), absolute ethanol (25 c.c.), and potato starch (56 g.) were added at 0° to 2°. The whole was slowly stirred at +2° for 24 hours, and the starch removed on the centrifuge in pots previously cooled to 0°. To the supernatant liquid (77 c.c.), cooled to 0° to −3°, cold acetone (154 c.c.) was added, with stirring, and the precipitate rapidly centrifuged off in pots previously cooled to <0°. The precipitate was dried by washing it in the centrifuge pots with two volumes (*ca.* 60 c.c. each) of cold acetone and finally in a vacuum-desiccator over phosphoric oxide. The dry powder (*ca.* 1·5 g.) was stored in the refrigerator. The phosphorylase activity of the preparation was equivalent to 1 unit in 430 mg. of the powder.

Determination of the Activity of R-Enzyme Preparations.—β-Dextrin (B.V. 0·145; dry wt. *ca.* 48 mg.) was moistened with ethanol, 0·012N-sodium hydroxide (15 c.c.) added, and dissolution completed by warming for 1 minute on a boiling water-bath. The solution was cooled, exactly neutralised to phenolphthalein with dilute sulphuric acid, and diluted to 25 c.c. (all subsequent polysaccharide solutions were prepared in the same manner). A portion, such that the remaining solution contained 46·7 mg. of β-dextrin, was removed, and the remainder diluted to 25 c.c.

A digest containing β-dextrin solution (3·75 c.c.), 0·2M-citrate buffer (pH 7·0; 1·5 c.c.), water (0·75 c.c.), and R-enzyme solution (0·028 g.; 1 c.c.) was incubated at 21°. At intervals portions (0·5 c.c. ≡ 0·5 mg. of β-dextrin) were removed and stained with iodine (1 mg.)–potassium iodide (10 mg.) in a final volume of 50 c.c. for determination of the blue value. The time taken for the blue value to increase from 0·150 to 0·200 was taken as a measure of the activity.

The first sample of R-enzyme retained 85% of its original activity after storage for 11 weeks.

Experiments to show that the R-Enzyme is still Active when the β-Dextrin has reached the Maximum Blue Value.—A β-dextrin digest, prepared as described above, was incubated at 21° and, at intervals, portions (0·5 c.c.) were removed for determination of the blue value, the results being shown in Table I.

Table I.

The Action of R-enzyme on β-dextrin.

Digest A. β-Dextrin + R-enzyme.
Digest B. β-Dextrin + a portion of digest A after incubation for 28 hours.

Digest A	Time of incubation (hrs.)	0	1	3	4·8	10·5	22·7	34
	Blue value	0·142	0·178	0·218	0·242	0·265	0·270	0·265
Digest B	Time of incubation (hrs.)	0	2	19·5	23·5	46·3	—	—
	A.V. (680 mμ.)	0·183	0·198	0·249	0·253	0·270	—	—

After 28·3 hours a portion (1 c.c.) of this digest was used as enzyme for a second similar digest. Portions (0·5 c.c.) of this were removed and the A.V. (680 mμ.) determined after staining with iodine (1 mg.)–potassium iodide (10 mg.) in a total volume of 50 c.c. The results are also shown in Table I.

Determination of the Optimum pH.—A freeze-dried Q3-preparation (1·11 g., isolated from 75 g. of beans) was dissolved in water (50 c.c.), and ammonium sulphate solution (50 g./100 c.c.; pH 7·0) added, at 0°, to a concentration of 19 g./100 c.c. After storage for 30 minutes at 0° the precipitate was removed in cold centrifuge pots, dissolved in water (25 c.c.) containing sodium sulphate (0·25 g.), and centrifuged. The solution was then cooled to +2°, cold absolute ethanol (6·25 c.c.) and potato starch (14 g.) were added, and the whole was slowly stirred at +2° for 20¼ hours. The starch was removed on the centrifuge, and portions (1 c.c.) of the supernatant liquid were added to digests containing β-dextrin (7 mg.; 3·75 c.c.), sodium acetate–sodium veronal buffer (1·5 c.c., the pH being adjusted to six values between 2 and 9 by the addition of 0·1N-sulphuric acid), and water (0·75 c.c.) to give a total volume of 7 c.c. The digests were incubated at 21°, and at intervals portions (1 c.c.) removed for determination of the blue values. It is thus shown that the optimum pH is 6·5—7·0.

Determination of the Optimum Temperature.—β-Dextrin digests, prepared as under " Determination of the Activity " were incubated at four temperatures between 10° and 45°. At intervals portions (1 c.c.) were removed for determination of blue values. The optimum temperature is *ca.* 34°.

Action of R-Enzyme on β-Dextrin in the Presence of Phosphate Ions.—An R-enzyme solution (140·1 mg.; 5 c.c.) was centrifuged to remove a little insoluble residue, and portions (2 c.c.) were added to two digests: (A) contained β-dextrin (14 mg.; 7·5 c.c.), 0·2M-citrate buffer (pH 7·0; 3 c.c.), and water (1·5 c.c.) to give a final volume of 14 c.c. In (B) the citrate buffer was replaced by 0·2M-phosphate buffer (pH 7·0; 3 c.c.). The digests were incubated at 21°, and at intervals portions (1 c.c.) were removed for determination of the blue values. No difference was observed (Table II).

TABLE II.

The action of R-enzyme on β-dextrin in the presence and absence of inorganic phosphate ions.

Time of incubation (hrs.).	Blue values. Phosphate buffer.	Citrate buffer.	Time of incubation (hrs.).	Blue values. Phosphate buffer.	Citrate buffer.
0	0·142	0·142	26	0·247	0·255
2	0·190	0·185	32½	0·259	0·260
6½	0·226	0·226			

Successive Actions of R-Enzyme at pH 7·0, *and β-Amylase at* pH 4·8 *on Starch and Starch Fractions.*—β-Amylase, prepared from soya beans by the method given in Part II (*J.*, 1945, 882), was dissolved in 0·2M-acetate buffer, pH 4·8, to give an activity of 440 units/c.c., the insoluble residue being removed on a centrifuge. All solutions of β-amylase used in this work were prepared in the same manner.

A neutral solution of the polysaccharide under examination (1 mg./c.c.) was incorporated in digests as follows, all of which contained 0·2M-acetate buffer (pH 7·0; 3 c.c.):

Digest 1. Polysaccharide solution (10 c.c.); R-enzyme solution (2 c.c.; 56 mg.).

Digest 1*a*. The same.

Digest 2. Polysaccharide solution (10 c.c.); water (2 c.c.).

Digest 3. β-Dextrin (10 mg.; 10 c.c.); R-enzyme solution (2 c.c.).

The digests were incubated at 21°, and at intervals portions (0·75 c.c.) of (1*a*) and (3) were removed for determination of the blue values. At 21 hours the blue values of digests (1) and (2) were similarly determined to ensure that all the digests were proceeding at the same rate, and these digests were then heated on a boiling water-bath for 10 minutes to deactivate the enzyme. After cooling, the pH was adjusted to 4·8 by the addition of N-acetic acid (0·35 c.c.), and β-amylase solution (2 c.c.) and water to 25 c.c were then added. The digests were incubated at 35·5° and at given times portions (5 c.c.) were removed and the reducing power, as maltose, was determined after deproteinisation.

Blank digests, corresponding to (1) and (2), but containing no polysaccharide, were treated in the same way and used for the determination of the reducing power of the enzyme solutions. The results are recorded in Table III.

TABLE III.

The successive actions of R-enzyme and β-amylase on potato starch fractions.

Fraction.	Action of R-enzyme (21 hrs.) at pH 7·0. Initial B.V.	Final B.V.		Conversion into maltose by β-amylase (%) at pH 4·8. Time (hrs.). 7.	24.	33.	46.
β-Dextrin	0·145	0·265	(*a*)	2·8	5·4	6·0	7·0
			(*b*)	61·6	65·9	68·9	72·7
Amylopectin	0·160	0·246	(*a*)	48·3	51·1	52·3	53·5
			(*b*)	66·0	71·0	72·6	74·0
Starch	0·435	0·490	(*a*)	56·9	60·3	60·8	61·1
			(*b*)	71·0	77·7	78·4	79·2
Amylose I	0·910	0·860	(*a*)	66·5	70·3	71·3	71·3
			(*b*)	71·3	72·8	74·1	75·0
Amylose II	1·30	1·13	(*a*)	82·6	83·0	83·0	82·6
			(*b*)	78·4	81·0	82·7	85·3

Conversions: (*a*) Before the action of R-enzyme.
(*b*) After the action of R-enzyme.

Simultaneous Action of R-Enzyme and β-Amylase on β-Dextrin at pH 5·3.—Digests were prepared containing (1) β-dextrin (10 mg.; 10 c.c.), and β-amylase in aqueous solution (2 c.c.), (2) β-dextrin (10 c.c.), β-amylase (2 c.c.), and R-enzyme (2 c.c.; 56 mg.), and in addition both contained 0·2M-acetate buffer (pH 5·3; 3 c.c.) and water to 25 c.c. The digests were incubated at 35·5°, and at intervals the reducing power, as maltose, was determined on portions (5 c.c.) after neutralisation and deproteinisation. The results are recorded in Fig. 2.

Determination of the Reducing Power developed by R-Enzyme acting on β-Dextrin and Amylopectin.—Two digests were prepared containing (1) β-dextrin (28 mg.; 15 c.c.) and (2) amylopectin (B.V. 0·160; 28 mg.; 15 c.c.); in addition each contained R-enzyme (4 c.c.; 90·8 mg.), 0·2M-citrate buffer (pH 7·0; 6 c.c.), and water (3 c.c.).

The digests were incubated at 21°, and at intervals portions (0·5 c.c.) were removed for determination of the blue value, and further portions (4 c.c.) for determination of the reducing power as maltose after deproteinisation (Table IV). A control digest, as above, but containing water in place of the polysaccharide solution, was incubated in parallel for determination of the reducing power of the enzyme.

Change in Viscosity of β-Dextrin and Amylopectin Solutions during Incubation with R-Enzyme.—A solution of R-enzyme (27·6 mg./c.c.) was prepared, centrifuged, and placed in a thermostat at 21°. Two digests containing 0·2M-citrate buffer (pH 7·0; 1·5 c.c.), water (0·75 c.c.), and respectively amylopectin and β-dextrin (7 mg.; 3·75 c.c.) were also placed in the thermostat. When all had attained 21° the R-enzyme solution (1 c.c.) was added to the digests and, 1 minute after mixing, portions (2 c.c.) were transferred from each digest to Ostwald viscometers in the same thermostat. At intervals, portions (0·5 c.c.) were removed

from the main bulk of each digest for determination of blue value, and at the same time the time of flow of the liquid in the viscometer was observed. In addition to these digests, the times of flow of water and a control digest containing no polysaccharide were determined. See Fig. 1.

Amylopectin, before and after Incubation with R-Enzyme, as a Primer for Phosphorylase Synthesis.—Two digests were prepared both containing amylopectin (7 mg.; 3·75 c.c.), 0·2M-citrate buffer (pH 7·0; 1·5 c.c.), and water (0·75 c.c.). In addition (1) contained R-enzyme solution (29·4 mg.; 1 c.c.), and (2) water (1 c.c.). Both digests were incubated at 35·5° for 10½ hours, and a portion (0·5 c.c.) was removed from each for determination of blue value. A further portion (1 c.c.) of each was incorporated in a digest containing in addition 0·1M-glucose-1 phosphate (1 c.c.), 0·5M-citrate buffer (pH 6·0; 0·5 c.c.), and bean phosphorylase (4·4 units; 1 c.c.). The digests were incubated at 35·5° for 12 minutes, the enzyme was destroyed by the addition of 10% trichloroacetic acid (5 c.c.), the protein precipitate removed on the centrifuge, and the inorganic phosphate in a portion (1 c.c.) of the supernatant liquid determined. A control digest was used to determine the initial inorganic phosphate concentration. Table V shows the priming action to be unchanged.

TABLE IV.

The reducing power developed by R-enzyme alone acting on β-dextrin and amylopectin.

	β-Dextrin.		Amylopectin.	
Time of incubation (hrs.).	B.V.	Conversion into maltose (%).	B.V.	Conversion into maltose (%).
0	0·145	0·0	0·158	0·0
2	0·170	0·0	0·185	0·0
8	0·220	7·0	0·218	1·0
21½	0·266	11·2	0·245	1·3
25½	0·259	11·4	0·246	1·0

TABLE V.

The priming action of amylopectin in phosphorylase synthesis before and after treatment with R-enzyme.

Primer.	Inorganic phosphorus (mg.) liberated per c.c. of inactivated digest.
Amylopectin (B.V. 0·170)	0·036
Amylopectin treated with R-enzyme (B.V. 0·293)	0·030

Simultaneous Action of α-Amylase and R-Enzyme on Amylose. B.V.–% Conversion into Maltose.—A solution of amylose (B.V. 1·20) of concentration 14 mg./7·5 c.c. was incorporated in digests containing (1) amylose solution (15 c.c.) and salivary α-amylase (1 : 500 dilution; 4 c.c.), and (2) amylose solution (15 c.c.), a solution of R-enzyme (167·3 mg.), and α-amylase (4 c.c.). In addition each contained 0·2M-citrate buffer (pH 7·0; 6 c.c.) and water (3 c.c.). At intervals, portions (4 c.c.) were removed for determination of the reducing power as maltose after being deproteinised, and further portions (0·5 c.c.) for determination of blue values. Corrections were made for the intrinsic reducing powers of the enzymes. The results recorded in Fig. 3 show that R-enzyme does not influence the normal course of α-amylolysis.

Successive Actions of α-Amylase, R-Enzyme, and β-Amylase on Amylose.—Digest (1): Amylose (B.V. 1·20; 53·6 mg.) dissolved as usual; 0·2M-acetate buffer (pH 7·0; 5 c.c.); α-amylase (saliva diluted 1 : 100; 3 c.c.); and water to 50 c.c. The digest was incubated at 21° and at intervals portions (1 c.c.) were removed and stained with iodine (2 mg.)–potassium iodide (20 mg.) in a total volume of 100 c.c. for determination of the A.V. (680 mμ.). The results are given in Table VI.

TABLE VI.

Time (mins.)	0	5	17	55	75	195
A.V. (680 mμ.)	1·28 *	0·955	0·800	0·293	0·192	0·053

* Calculated value.

At the times shown in Table VII, portions (10 c.c.) were removed, placed in flasks (2), (3), (4), and (5) and heated in boiling water (10 minutes) and then cooled. To (2) and (4), 0·2M-acetate buffer (pH 7·0; 2 c.c.) and water (3 c.c.) were added, and to (3) and (5) 0·2M-acetate buffer (pH 7·0; 2 c.c.), water (1 c.c.), and R-enzyme (56 mg.; 2 c.c.). The digests were incubated at 21° for 19 hours.

TABLE VII.

Digests.	Time of removal of aliquot from digest (1) (mins.).	A.V. (680 mμ.) of digest (1).
(2) and (3)	14	0·835
(4) and (5)	65	0·237

At 19 hours, digests (2), (3), (4), and (5) were heated in boiling water (10 minutes), then cooled, and N-acetic acid (0·35 c.c. to adjust to pH to 4·4), β-amylase (2 c.c.), and water to 25 c.c. were added. The digests were incubated at 35·5°, and at intervals portions (5 c.c.) were removed for determination of the reducing power as maltose, after deproteinisation. Controls containing water in place of the polysaccharide

gave the reducing power of the enzymes alone. To ensure that the R-enzyme was fully active, it was incubated with β-dextrin. The results are recorded in Table VIII.

TABLE VIII.

The successive actions of α-amylase, R-enzyme, and β-amylase on amylose.

B.V. of dextrins produced by α-amylase at pH 7·0.		Conversion into maltose by β-amylase at pH 4·8, %. 5 hrs.	8 hrs.
0·827	*a*	78·7	81·2
	b	83·1	85·6
0·221	*a*	85·6	86·7
	b	81·8	83·1

Conversions: (*a*) Before the action of R-enzyme at pH 7·0.
(*b*) After the action of R-enzyme at pH 7·0.

Synthesis of a Polysaccharide from Glucose-1 Phosphate by Phosphorylase in the Presence of R-Enzyme.—A primer was prepared by hydrolysing amylose (B.V. 1·43; 20 mg.) with sulphuric acid to the achroic point. The solution was neutralised and diluted to 10 c.c. Two digests were prepared, both containing 0·5M-citrate buffer (pH 6·0; 2 c.c.), potato phosphorylase (P4, activity 3·3 units; 2 c.c.), primer solution (0·25 c.c.), 0·1M-glucose-1 phosphate (1 c.c.). In addition, digest (2) contained water (0·75 c.c.) and R-enzyme (28·0 mg.; 1 c.c.), and digest (1) water (1·75 c.c.). The digests were incubated at 21°, and at intervals portions (1 c.c.) stained with iodine (2 mg.)–potassium iodide (20 mg.) in a total volume of 100 c.c. for determination of A.V. The results are recorded in Table IX.

Successive Actions of R-Enzyme, Potato Q-Enzyme, and Soya β-Amylase on β-Dextrin.—A new β-dextrin preparation was used in this experiment. The results are therefore not directly comparable with those given in Table III.

TABLE IX.

The synthesis of a polysaccharide from glucose-1 phosphate by phosphorylase in the presence of R-enzyme.

Time of incubation (hr.).	A.V. (680 mμ.). Enzymes. P- + R-.	P- alone.	Time of incubation (hr.).	A.V. (680 mμ.) Enzymes. P- + R-.	P- alone.
1	0·148	0·134	10·7	1·48	1·48
2·5	0·512	0·496	22·7	1·67 *	1·75
4·5	0·875	0·860	34·3	1·33 *	1·62 *

* Precipitate forming.

The R-enzyme solution contained 28 mg./c.c. and the Q3-solution 109·9 mg./4·5 c.c. Digests were prepared, all of which contained β-dextrin (18·7 mg.; 10 c.c.), 0·2M-acetate buffer (pH 7·0; 3 c.c.), and water (3·7 c.c.). In addition digest (1) contained water (2 c.c.), and digests (2) and (3) R-enzyme solution (2 c.c.). The digests were incubated at 21° for 21 hours, then portions (0·5 c.c.) were removed for determination of B.V. and the enzyme was destroyed by heat. After cooling, to each was added 0·2M-acetate buffer (pH 7·0; 1 c.c.); in addition, to digest (2) was added Q-enzyme solution (2 c.c.), and to each water to 25 c.c. These digests were incubated at 21° for 6 hours and after removal of portions (0·69 c.c.) for determination of B.V., the digests were heated in boiling water for 10 minutes. The β-amylolysis limits at pH 4·8 of portions (20 c.c.) of each were determined in the usual way. The results are recorded in Table X.

TABLE X.

The successive actions of R-enzyme, Q-enzyme, and β-amylase on β-dextrin.

	B.V.	β-Amylolysis (% conversion) after: 5 hrs.	7 hrs.	16 hrs.
(*a*) β-Dextrin	0·172	4·9	4·9	4·9
(*b*) R-Treated β-dextrin	0·308	68·7	71·4	71·4
(*c*) After Q-enzyme action on (*b*)	0·207	65·9	66·8	67·7

Successive Actions of R-Enzyme, Potato Q-Enzyme, and β-Amylase on Amylopectin.—The procedure given above was followed throughout, the β-dextrin being replaced by amylopectin. The results are given in Table XI.

TABLE XI.

	B.V.	β-Amylolysis (% conversion) after: 4 hrs.	18 hrs.	20 hrs.
(*a*) Amylopectin	0·148	50·5	51·1	—
(*b*) R-Treated amylopectin	0·255	67·3	65·8	—
(*c*) After Q-enzyme action on (*b*)	0·140	61·2	63·2	63·2

Action of Bean Q-Enzyme on β-Dextrin at pH 5·2.—A freeze-dried Q3-preparation (176·4 mg.) was dissolved in 0·2M-acetate buffer (pH 4·8; 3 c.c.), and after being centrifuged a portion (2 c.c.) was added to a β-dextrin digest of the same volumes as the standard digest but containing 0·2M-acetate buffer (pH 4·8) in place of the citrate buffer. The presence of citrate buffer in the freeze-dried Q3-preparation gave a final pH value of 5·2. The digest was incubated at 21° and portions (1 c.c.) were removed at intervals for the determination of A.V. (680 mμ.). The results in Table XII show the presence of R-enzyme in the bean preparation.

TABLE XII.

The action of bean Q-enzyme on β-*dextrin at* pH 5·2.

Time of incubation (mins.)	1	30	58	109	927
A.V. (680 mμ.)	0·326	0·406	0·448	0·460 *	0·248 *

* Precipitate forming in digest.

We record our indebtedness to Mrs. Olive Owen (working under the auspices of the Colonial Products Research Council) for technical assistance, to Imperial Chemical Industries Limited for financial assistance, and to the Department of Scientific and Industrial Research for a grant to one of us (P. N. H.).

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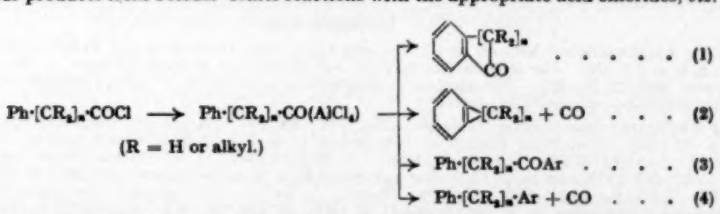
334. *The Reaction between Aromatic Compounds and Derivatives of Tertiary Acids. Part VI.* The Simultaneous Formation of Open-chain and Cyclic Ketones from Some Alkylated Phenylpropionyl Chlorides.*

By EUGENE ROTHSTEIN.

Increasing proportions of open-chain ketones are produced when β-phenylpropionyl chloride or its derivatives methylated in the side-chain are treated with aluminium chloride in the presence of increasingly reactive aromatic derivatives. This is also observed when the concentration of the last is raised. On the other hand, increasing alkylation has the opposite effect, and with β-phenyl-ααβ-trimethylbutyryl chloride the sole product is 2 : 2 : 3 : 3-tetramethylindanone.

THE inference that the preferential cyclisation usually observed with derivatives of β-phenylpropionyl chloride is caused by the proximity of the acyl group to the benzene nucleus (Part I, Rothstein and Saville, *J.*, 1949, 1946) leads to the reasonable conclusion that open-chain ketones should be formed in the presence of sufficiently " activated " aromatic compounds. Without necessarily implying the identity of the mechanisms of the following reactions, it is possible to envisage four products from Friedel–Crafts reactions with the appropriate acid chlorides, *viz.* :

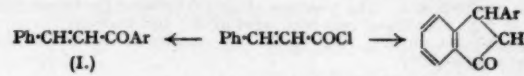


The simultaneous appearance of all four substances has not yet been encountered. Reactions (3) and (4) have been previously described (*J.*, 1949, 1950); reaction (2) will be the subject of a future communication. The present paper deals with the influence of substituent methyl groups on the relative amounts of the ketones isolated in reactions (1) and (3) where $n = 2$.

There are few recorded cases where open-chain ketones are formed from aralkyl acid halides. The most extensive work has been carried out with cinnamoyl chloride (for comprehensive references see Thomas, " Anhydrous Aluminium Chloride in Organic Chemistry "), the products being the chalkone (I) and the 3-arylindan-1-one (II), the proportions depending mainly on the

* Part V, *J.*, 1949, 1961.

substituent groups in the aryl component ArH. The course of the reaction has been examined by Kohler (*Amer. Chem. J.*, 1909, **42**, 376) but has not been fully clarified.



It is well known that β-phenylpropionyl chloride usually yields the indanone, but open-chain ketones are obtained by reaction with phenols (Shinoda *et al.*, *J. Pharm. Soc. Japan*, 1931, **51**, 23, 78; Mayer and Zütphen, *Ber.*, 1924, **57**, 200), or anisole (Winternitz and Mouseron, *Bull. Soc. chim.*, 1948, 567). The effect of substitution in the side-chain carrying the acid chloride group has not previously been investigated, and the results now obtained are tabulated below.

Yield of open-chain ketones from the Friedel–Crafts reaction with alkylated β-phenylpropionyl chlorides.

Expt. no.	Substituents.	Aromatic component, mols. %.*	Yield of products, %.	Open-chain ketone (mols. %) in mixture.
1	Unsubstituted	Benzene, 100	—	0·0
2	,,	Anisole, 16	85·0	100·0
3	,,	Toluene, 100	90·1	32·7
4	αα-Me_2	Benzene, 100	—	0·0
5	,,	Anisole, 16	83·8	9·0
6	,,	,, 41	100·0	30·0
7	,,	,, 100	92·4	64·0
8	,,	Toluene, 100	92·2	0·0
9	ααββ-Me_4	Benzene, 100	—	0·0
10	,,	Anisole, 100	100·0	0·0

* In benzene (where appropriate).

It is evident that an increase in the reactivity of the aromatic derivative (cf. Part II, *loc. cit.*) raises the proportion of open-chain ketone. This is particularly noticeable with β-phenylpropionyl chloride when the solvent is changed from benzene (complete cyclisation) to toluene or anisole (experiments 1—3). The opposite effect of successive alkylation can be observed when the reactions in pure anisole are compared. Cyclisation which is negligible in the case of β-phenylpropionyl chloride even when only 16% of anisole is present is the sole reaction with β-phenyl-αββ-trimethylbutyryl chloride (experiments 2, 7, and 10). It is consistent with the second-order kinetics associated with the formation of ketones (*J.*, 1949, 1959) that an increase in the concentration of anisole results in larger proportions of the non-cyclic product although in the case of the dimethylated acid chloride no more than 64% is obtained even in pure anisole solution (experiments 5—7). No appreciable quantities of carbon monoxide were eliminated in the reactions studied in this work; this conforms with the arguments advanced in Part I that the relatives rates of reaction are (1) > (3) > (4).

Experimental.

The undermentioned ketones and their derivatives were isolated in the Friedel–Crafts reactions nos. 2, 3, and 5—10. The semicarbazones were best prepared in pyridine (Hopper, *J. Roy. Tech. Coll., Glasgow*, 1929, **2**, [i], 52). This method eliminated the so-called steric effects usually encountered in highly alkylated carbonyl compounds.

p-β-Phenylpropionylanisole (Jörlander, *Ber.*, 1917, **50**, 406) crystallised from ether, light petroleum (b. p. 60—80°), or absolute alcohol in thick plates, m. p. 101—102° (previous workers reported 97°) (Found: C, 80·1; H, 6·3. Calc. for $C_{16}H_{14}O_2$: C, 80·0; H, 6·7%). The oxime (Pfeiffer and Negreanu, *Ber.*, 1917, **50**, 1477) had m. p. 115° after recrystallisation from 95% alcohol (Found: C, 75·5; H, 6·8; N, 5·3. Calc. for $C_{16}H_{17}O_2N$: C, 75·3; H, 6·7; N, 5·5%). The *semicarbazone* separated from the same solvent in needles, m. p. 135° (Found: C, 68·6; H, 6·4; N, 14·2. $C_{17}H_{19}O_2N_3$ requires C, 68·7; H, 6·4; N, 14·1%).

p-β-Phenylpropionyltoluene (obtained by Burton and Ingold by a different method; *J.*, 1928, 916), b. p. 145°/0·1 mm., crystallised from light petroleum (b. p. 60—80°) and had m. p. 70—71° (Found: C, 85·3; H, 7·1. Calc. for $C_{16}H_{16}O$: C, 85·7; H, 7·2%). The oxime was recrystallised twice from dilute alcohol and then had m. p. 99° (Found: C, 80·1; H, 6·9; N, 5·7. Calc. for $C_{16}H_{17}ON$: C, 80·3; H, 7·1; N, 5·9%). The semicarbazone, crystallised from alcohol, had m. p. 138—139° (Found: C, 73·0; H, 6·9; N, 15·0. Calc. for $C_{17}H_{19}ON_3$: C, 72·6; H, 6·8; N, 14·9%). Burton and Ingold (*loc. cit.*) give the m. p. for the oxime as 101°, and that of the semicarbazone as 135—137°.

β-p-*Anisoyl-α-phenylisobutane*, b. p. 151°/0·1 mm. (Found: C, 80·4; H, 7·6. $C_{18}H_{20}O_2$ requires C, 80·6; H, 7·5%). The *oxime* separated from absolute alcohol in needles, m. p. 157° (Found: C, 76·1; H, 7·3; N, 5·0. $C_{18}H_{21}O_2N$ requires C, 76·3; H, 7·4; N, 4·9%). Recrystallisation of the *semicarbazone*

from 95% alcohol afforded prisms, m. p. 156—157° (Found: C, 70·0; H, 7·1; N, 12·9. $C_{15}H_{22}O_2N_2$ requires C, 70·2; H, 7·2; N, 12·9%).

2 : 2-Dimethylindan-1-one, b. p. 64°/0·1 mm., m. p. 45—46° [after recrystallisation from light petroleum (b. p. 40—60°)] (Found: C, 82·5; H, 7·8. Calc. for $C_{11}H_{12}O$: C, 82·5; H, 7·8%). The m. p. of the semicarbazone was somewhat indefinite (180—203°), though any particular specimen melted sharply within this range and gave a satisfactory analysis (Found, for a sample of m. p. 203°, twice crystallised from alcohol: C, 66·3; H, 6·9; N, 19·2. Calc. for $C_{12}H_{15}ON_3$: C, 66·4; H, 7·0; N, 19·3%). The recorded m. p. is 209° (Haller and Bauer, *Ann. Chim.*, 1921, [ix], **16**, 340). The discrepancy may be caused by the formation of geometrical isomerides. No difficulty was encountered with the *oxime* which separated from dilute alcohol in prisms, m. p. 115° (Found: C, 75·0; H, 7·6; N, 8·2. $C_{11}H_{13}ON$ requires C, 75·4; H, 7·4; N, 8·0%).

Friedel–Crafts Reactions.—(2) Freshly prepared aluminium chloride powder (10 g., 3/40 mol.) was dissolved in a mixture of benzene (30 c.c.) and anisole (11 c.c.). A solution of β-phenylpropionyl chloride (8·4 g., 1/20 mol.) in benzene (15 c.c.) was added with stirring during an hour at room temperature. The mixture was warmed for an hour at 50°, decomposed by ice and dilute hydrochloric acid, and extracted with benzene.

(3) Toluene as the only solvent gave a homogeneous liquid only after the addition of the acid chloride. The products were indan-1-one (4 g.), b. p. 73°/0·2 mm., needles, m. p. 42°, from light petroleum (b. p. 40—60°), and *p*-β-phenylpropionyltoluene (3·3 g.).

(5) Use of pivaloyl chloride (10 g.) led to a clear red liquid which afforded 2 : 2-dimethylindan-1-one (6·1 g.) and 2-*p*-anisoyl-1-phenyl*iso*butane (1 g.).

(6) The acid chloride was added in anisole solution. The yields of indan-1-one and open-chain ketone were 5·7 and 4·1 g. respectively.

(7) The usual quantities gave 2·65 and 7·95 g. of the respective products. An experiment starting with 23 g. of the acid chloride led to similar yields (5·8 and 20·8 g.).

(8) The indanone (8·7 g.) was the only product from this reaction.

(10) *aaβ*-Trimethyl-β-phenylbutyric acid (14 g.) (from tetramethylsuccinic anhydride, Rothstein and Saboor, *J.*, 1943, 425) was converted into the acid chloride, b. p. 127—128°/7 mm. (12·2 g., 80%), by using a slight excess of thionyl chloride. The reaction in anisole solution furnished 2 : 2 : 3 : 3-tetramethylindan-1-one, b. p. 80—81°/0·1 mm. in theoretical yield (Found: C, 82·8; H, 8·7. Calc. for $C_{13}H_{16}O$: C, 83·0; H, 8·5%). This substance had been previously prepared by Rothstein and Saboor (*loc. cit.*) by cyclising the acid itself with concentrated sulphuric acid. They had been unable to isolate any carbonyl derivatives but with the larger quantities of the pure material now available there have been prepared a *semicarbazone*, flat prisms (from 95% alcohol), m. p. 206° (Found: C, 68·6; H, 7·5; N, 16·9. $C_{14}H_{19}ON_3$ requires C, 68·6; H, 7·8; N, 17·1%), and an *oxime*, plates (from alcohol), m. p. 143—144° (Found: C, 77·1; H, 8·6; N, 6·9. $C_{13}H_{17}ON$ requires C, 76·8; H, 8·4; N, 6·9%).

Analyses were by Dr. G. Weiler and Dr. F. B. Strauss of Oxford.

THE UNIVERSITY, LEEDS. [*Received, February 2nd*, 1951.]

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335. *Separation of Yttrium and Erbium with the Aid of Ethylenediaminetetra-acetic Acid ("Enta Acid").*

By J. K. MARSH.

Yttrium–erbium oxalate is dissolved in diammonium dihydrogen enta and ammonia to give a somewhat acid solution, and is then fractionally precipitated by acidification. Rapid concentration of yttrium occurs in the precipitate. With excess of enta present, oxalate crops can be obtained by cooling hot saturated solutions. After initial spreading, crops are ignited and the oxides dissolved in appropriate mother-liquors, thus stabilising the pH for conducting a continuous fractionation. Erbium is obtained free from yttrium without difficulty, and is separable from enta acid without appreciable loss.

THE main object of this work has been to establish a practicable procedure for the use of "enta" in separating the lanthanons. The wide range of stability of the complexes formed by various earths probably makes a number of individual modifications necessary, but it is important to be able to recover the lanthanons at will. Owing to the complex-forming power of enta, this is unusually difficult, since oxalate or hydroxide precipitation, though normally acting quantitatively, here breaks down.

The separation of yttrium and erbium was chosen for particular study since erbium gives the more stable complexes and is strongly coloured. Its detection by eye or spectroscope is therefore easy, and risk of loss in rejected products is small.

In a previous paper (*J.*, 1950, 1819) the fractional precipitation of a batch of earths as oxalate in presence of enta was reported. A rather different procedure is now described. The precipitation of lanthanon oxalate may occur under widely varying conditions, *e.g.*, (1) from neutral solutions of simple ionic salts, from which precipitation is immediate and only slightly selective; (2) from complex alkaline or neutral solutions holding oxalate to capacity for the amount of complex-forming agent present, from which addition of a simple lanthanon salt solution causes precipitation of oxalate with moderate selectivity of the stronger bases; (3) from solutions highly charged with complex-forming agent (alkali enta), precipitation from which is best brought about by sufficient acid to cause partial decomposition of the soluble complex with production of free $Ln^{\cdots}$ and oxalate ions up to the concentration permitted by the solubility product for lanthanon oxalate. The complex stability is affected primarily by pH and the nature of the lanthanon. Hence, for a pair of lanthanons of different basic strength, the weaker base will give the more stable complex, and the most suitable pH for selective precipitation of the stronger base will be that at which the stabilities differ most widely. In too alkaline a solution both components may be nearly fully converted into complexes, and precipitation occurs through inability of the complex-forming agent to hold oxalate in solution as in (2) above. In the acid range there is preferential decomposition of the complex of the stronger base.

For yttrium–erbium mixtures, it is best to use solutions at a pH not much higher than that at which enta acid will be precipitated. Half a given supply of lanthanon oxalates is dissolved in ammoniacal enta to give a neutral solution, and then precipitated fractionally at the boil by addition of enta, oxalic, or hydrochloric acid. Addition of enta acid will lower the pH without at first producing an oxalate precipitate. Its use at this stage allows of an adjustment of pH to a suitable value. Oxalic acid brings about precipitation without a sharp change in pH as the lanthanon passes from anionic to cationic binding. Much buffering may also take place by formation of acid ammonium oxalates; thus a point comes when addition of oxalic acid precipitates only a little oxalate. At this stage the liquor is sufficiently acid to dissolve a quantity of fresh lanthanon oxide. This is derived from the reserved half of the original batch of oxalates, and may be converted into complex in two or three portions as shown in the Table,

Initial separation of yttrium–erbium oxide (53% *erbium*).

Crop.	Wt., g.	Analysis of oxide. Er_2O_3, %.	pH of mother-liquor.	Remarks.
1	37	27·6	4·56	—
2	38	36·0	4·70	—
3	71	59·0	4·10	45 G. of fresh oxide dissolved in mother-liquor.
4	26	35·2	4·00	26 G. " " "
5	38	38·6	3·82	—
6	35	45·0	3·66	—
7	48	54·0	—	Contained enta acid.
8	35	75·4	—	—
9	82	89·5	—	About 60% of free enta acid.
10	55	97·6	—	" 80% " "
11	57	96·5	—	Contained ammonium tetroxalate and only a little erbium oxalate.

producing a rise in pH of the solution and permitting further oxalate crops to be obtained. The last stage of the precipitation is best carried out by addition of hydrochloric acid. This effectively decomposes the complex, and precipitates a mixture of lanthanon oxalate and free enta acid. The resolution of this mixture is described in the Experimental section.

The initial oxalate crops are separately converted into complex with fresh ammonium enta solution, and partly reprecipitated with oxalic acid. The resulting oxalate crops are ignited to oxide, and dissolved in the appropriate mother-liquors to be submitted to a fractionation on 6—8 fractions at a pH of 4—6.

There is a region of enta/oxalate ratio where a difference of oxalate solubility with temperature arises. This varies with different earths, being higher in the cerium group than with erbium. Thus it comes about that, in the more highly acid ranges of solutions, precipitation of oxalates can be brought about either by the addition of oxalic or hydrochloric acid to the boiling solution till a crop is obtained, or by addition till precipitation is only incipient, and the oxalate crop is formed on cooling. There is not much difference in separational effectiveness of the two methods.

The cooling method gives crops of enta acid at an earlier stage or an ammonium oxalate according to conditions, and so is less satisfactory in the higher acid ranges.

Complete elimination of yttrium from erbium has been obtained on a small sample, but the comparative merits or enta and the ferricyanide method (Marsh, *J.*, 1947, 118) for purifying erbium cannot yet be assessed. Holmium and yttrium are not separated efficiently by the use of enta, but are by ferricyanide. A mixture of yttrium and erbium containing a little holmium should therefore yield pure erbium more efficiently by use of enta than by ferricyanide.

Experimental.

The material used consisted of mixed yttrium and erbium oxides containing 53% by weight of the latter, and free from other lanthanons. Half of the oxide (71 g., 0·25 mol.) was converted into oxalate and dissolved in the necessary minimum of ammoniacal enta (= 125 g. of enta acid) to give an approximately neutral solution. This was diluted to 2 l., and enta acid added at the b. p. till precipitation of oxalate was incipient. The solution was then left to cool overnight. Crop 1 (see table) of oxalate was then collected, the filtrate re-boiled, and oxalic acid added till precipitation of oxalate was again incipient. After crop 3 the solution, which was now becoming acid, was treated with $(Y, Er)_2O_3$ run in as a thin cream as long as it dissolved readily upon being boiled for a few minutes. Cropping of oxalate then proceeded as before, but the solution became too acid after crop 6, and crop 7 contained free enta acid. Crop 8 was taken by adding sufficient oxalic acid to obtain an oxalate crop near the b. p. This was collected without cooling, and was free from enta acid. However, crops 9 and 10, taken similarly, again contained enta acid. On cooling, crop 11 consisted chiefly of an ammonium oxalate. The mother-liquor from crop 11 was divided, and part treated with oxalic acid and part with hydrochloric acid. The hydrochloric acid at once precipitated the remaining erbium, which however was very little. It was evident that hydrochloric acid was preferable to an excess of oxalic acid and was used subsequently.

Successful working of the process depends upon the separation of oxalate and enta acid. The latter is only slightly soluble in cold water, but readily gives hot supersaturated solutions. When the reaction liquor first shows signs of depositing enta acid near the b. p., it is useful to dilute it several-fold. Further acidification with hydrochloric acid is then made just so long as oxalate continues to be precipitated thereby. This oxalate is collected at once, and the liquor left to cool and for 1—2 days. It deposits enta acid mixed with a little oxalate. The mother-liquor then contains only a trace of erbium and very little enta acid; if further acidification and standing produce no further crop, the liquid can be rejected safely.

The procedure described results in crops of nearly pure oxalate which are ignited without difficulty, and a crop of enta acid with some oxalate. When this crop is treated with successive small amounts of cold dilute ammonia, the oxalate forms a complex and passes into solution. It is filtered off, leaving much the greater part of the enta acid pure, as may be proved by bringing it into solution with alkali and examining it for erbium absorption bands. The erbium which has passed into solution is reprecipitated as oxalate as before.

Further working of the crops thus obtained was done by the fractional process already described. The oxalates sometimes contained a little enta, and upon ignition gave a rather vitreous form of oxide which had to be ground wet before it was redissolved in the acid mother-liquors.

The oxalate–enta complex could be obtained as 10-faced monoclinic crystals having the appearance of truncated octahedra of 3—4 mm. diameter, but on long storage one solution deposited prismatic crystals 1 cm. or more long of radiating habit.

The analyses of erbium oxides were made spectrophotometrically on perchlorate solutions, as recommended by Moeller and Brantley (*Anal. Chem.*, 1950, **22**, 433), but even so readings were found to increase by up to 10% on ageing.

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336. *The Adsorption Isotherm of Langmuir and of Brunauer, Emmett, and Teller for Multilayers where* n = 3.

By D. C. Jones.

An analysis of the adsorption isotherm of Langmuir and of Brunauer, Emmett, and Teller for multilayers, where the number of such layers is limited to 3, is made. The isotherms are shown to change from Type I through IV and V and then to V$_A$ as the values of c change from just greater than 2·16 to *ca.* 0·25. *Three* is thus the smallest value of n where all the known isotherm types for a limited number of multilayers can be encountered as c varies. At high values of c ($c > 1000$) the change of adsorption type from I to IV again occurs in this case. The $x/(V/V_m)$ against x curves are analysed, especially in relation to approximations which hold at low values of x.

It has been shown recently (Jones and Birks, *J.*, 1951, 1127) that an analysis of the case when $n = 2$ in the Langmuir–Brunauer, Emmett, and Teller (B.E.T.) theories for multilayer adsorption leads to realisable isotherms which change from Type I to Type V as the value of c changes from $c > 2$ to $2 > c > ca.$ 0·2, and then to a type that may be called V$_A$ if $ca.$ 0·2 $> c > 0$. The case when $n = 3$ is analysed in this paper.

When $n = 3$ the Langmuir equation becomes

$$\frac{N\eta}{N_0} = \frac{\sigma_1\mu[1 + 2(\sigma_2\mu) + 3(\sigma_2\mu)^2]}{1 + \sigma_1\mu[1 + \sigma_2\mu + (\sigma_2\mu)^2]} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

and the Brunauer equation

$$\frac{V}{V_m} = \frac{cx(1 + 2x + 3x^2)}{1 + cx(1 + x + x^2)} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

These equations are identical if $\sigma_1\mu = cx$ and $\sigma_2\mu = x$; c then $= \sigma_1/\sigma_2$; σ_2 is considered equal to σ_3. It is not necessary to assume for the purpose of this analysis that $\sigma_2 = \sigma_L$ as in the further B.E.T. treatment.

From equation (2), $V/V_m = 0$ only when $x = 0$, the factor in parentheses in the numerator having no real roots. V/V_m approaches 3 as x approaches ∞ (see Jones, *J.*, 1951, 126).

$V/V_m = \infty$ if $1 + cx + cx^2 + cx^3 = 0$; this equation has no real positive roots ($c > 0$); if x is negative it can be shown that there is one real root; *i.e.*, V/V_m passes to infinity at one negative value of x only. This is typical of all cases in this model where n is an odd number, and may be contrasted with the cases where n is even, *e.g.*, $n = 2$ (Jones and Birks, *loc. cit.*).

Differentiating equation (2), we obtain

$$\frac{1}{c} \cdot \frac{d}{dx}\frac{V}{V_m} = \frac{1 + 4x + (c + 9)x^2 + 4cx^3 + cx^4}{[1 + cx(1 + x + x^2)]^2} \quad . \quad . \quad . \quad . \quad . \quad (3)$$

The numerator here, if equated to zero, has no real positive root ($c > 0$) and therefore for values of $x > 0$ no maximum or minimum occurs on the isotherm; such values do occur for values of $x < 0$. The gradient at the origin $= c$.

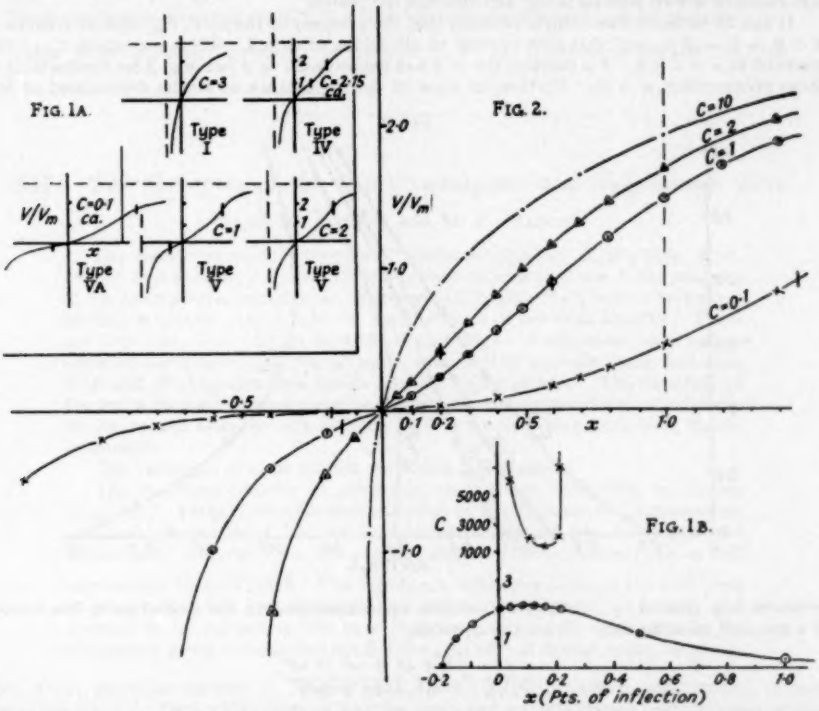
Differentiating again, we obtain

$$\frac{1}{c} \cdot \frac{d^2}{dx^2}\frac{V}{V_m} = \frac{(c - 2) + 3(c - 3)x + 3cx^2 - c(c - 17)x^3 + 3c(c + 6)x^4 + 6c^2x^5 + c^3x^6}{[1 + cx(1 + x + x^2)]^3} \quad . \quad (4)$$

The investigation of this equation for the occurrence of points of inflection on the isotherm can proceed best as follows: the sign changes of the coefficients of x ($x > 0$) as c varies can be considered from the point of view of Descartes's rule of signs (see, *e.g.*, "The Theory of Equations," J. V. Uspensky, McGraw-Hill, 1948, p. 121) which can give preliminary information as to the general location of the roots. If $0 < c < 2$ there is one sign change and therefore there is one real positive root only; if $c = 2$ the absolute term is zero, giving a root at the origin and, excluding zero, there is now one sign change, again giving one real positive root only; if $3 > c > 2$ there are two sign changes and therefore either two real positive roots or none; if $3 < c < 17$ there are no sign changes and therefore no positive roots, *i.e.*, between $c = 3$ and $c = 17$ there can be no points of inflection on the isotherm. But if c is greater than

17 the term in x^3 is negative and again there are two sign changes and therefore either two real positive roots or none. Descartes's rule of signs is of particular value in this case because of the small number of sign changes involved and by its aid alone the occurrences of points of inflection, and so of isotherm types, can be mapped out.

The actual positions of the points of inflection can then be located by a combination of the methods of solving the polynomial in x graphically, which will give values of x corresponding to chosen values of c, and of treating the equation as a quadratic in c, which will give values of c corresponding to chosen values of x. In this way the following results have been obtained (illustrated in Fig. 1A). If $c > ca.\ 2{\cdot}16$ there are no real positive roots (it will be shown later that this does not apply when $c > ca.\ 1000$); if $c = ca.\ 2{\cdot}16$ there are two equal positive roots when x has the value $ca.\ 0{\cdot}1$; if $2{\cdot}16 > c > 2$ the two roots separate, until when $c = 2$ one root is at the origin and the other at $x = ca.\ 0{\cdot}21$; if $2 > c > 0{\cdot}2$ one point of inflection is now at



negative values of x and the other at higher positive values of x; if $c = ca.\ 0{\cdot}25$, $x = 1$, and if $ca.\ 0{\cdot}25 > c > 0$ one point of inflection is negative and the other is at an x value greater than the saturation value (if $x = p/p_0$). For this case then there is the appearance on some of the realisable isotherms of two points of inflection, giving the type of curve that has been labelled by Brunauer Type IV, these two points having their genesis at $c = ca.\ 2{\cdot}16$ and then rapidly diverging as c gets smaller; the type changes involved are shown in Fig. 1A. This case does not occur when $n = 1$ (Type I only) or with $n = 2$ (see above). When $n = 3$ it occurs only within the narrow range of c values as described here; when $n > 3$ this range is widened.

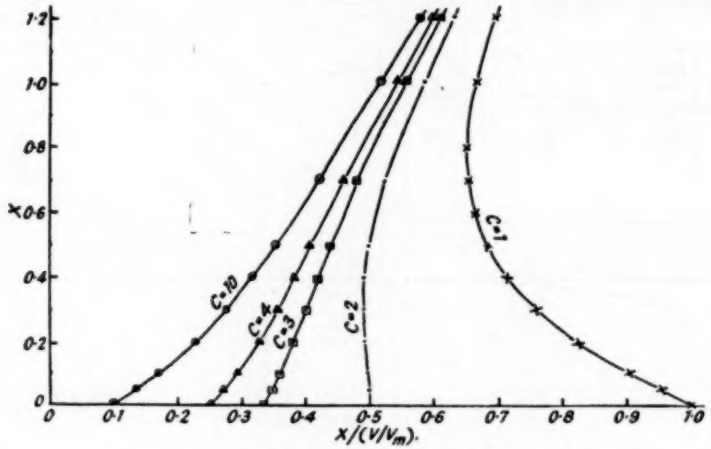
If $x > ca.\ 0{\cdot}226$, there are two real roots of c, one positive and one negative; if $ca.\ 0{\cdot}226 > x > 0$ there are two real positive roots of c, one of which (near $c = 2$) has already been discussed in this paper, and the other occurs when $c > 1100$. It has been found that the two positive roots have their genesis at a value of $c = ca.\ 1100$ corresponding to a value of $x = ca.\ 0{\cdot}16$; as c increases again these values diverge (apparently approaching the values of $x = 0$ and $x = 0{\cdot}226$). Thus at high c values a change of isotherm from Type I to Type IV

again occurs between certain x values, which however may be difficult to observe experimentally. In Fig. 1B the curves show the changes in the location of the points of inflection with changes in the value of c for this case. Attention should be drawn here to the fact that, as pointed out before (Jones, *loc. cit.*), this analysis would apply also to a monolayer (Langmuir's Case IV) where there are three molecules accommodated per elementary space and when $\sigma_1 \neq \sigma_2$ but $\sigma_2 = \sigma_3$.

In Fig. 2 are illustrated theoretical isotherms for typical values of c; and in view of the considerable use made by experimenters of the plots $x/(V/V_m)$ against x, which are of course tests of the agreement of the isotherm with a rectangular hyperbola whose asymptotes are parallel to the axes and which passes through the origin (compare Langmuir's Case I), these corresponding graphs are given in Fig. 3. For $n = 3$, as contrasted with $n = 2$, the isotherm is never a rectangular hyperbola, although in certain concentration ranges, as seen in Fig. 3, a straight line could be drawn passing fairly well through the points.

It can be deduced from simple calculus that the gradient of the $x/(V/V_m)$ against x curve at $x = 0$ is $(c - 2)/c$, and that this applies to all values of $n > 1$. Therefore when $c = 2$ the gradient at $x = 0$ is 0; it is positive if $c > 2$ and negative if $c < 2$ (see Fig. 3 for illustrations of these points when $n = 3$). Further, in view of the importance of results determined at low

FIG. 3.



pressures (*e.g.*, Foster, *J.*, 1945, 773), suitable approximations to the isotherms at low values of x are here investigated. From the equation

$$\frac{x}{V/V_m} = \frac{1 + cx + cx^2 + cx^3}{c(1 + 2x + 3x^2)}$$

it is seen that when $x = 0$, $x/(V/V_m) = 1/c$; dividing the bracketed factor in the denominator into the numerator, we obtain

$$\frac{x}{V/V_m} = \frac{1 + x(c - 2) + x^2(1 - c) + \ldots\ldots}{c} \quad \ldots\ldots \quad (5)$$

where there are further terms in the numerator involving higher powers of x. The same expression is obtained for all values of $n > 2$, for the terms involving x and x^2. [For $n = 2$ all the coefficients of x^2 and higher powers of x include the factor $(4 - c)$.] This means that for small values of x, where cx^2 can be neglected in comparison with cx, there is a linear relation whose gradient is $(c - 2)/c$ (the gradient at $x = 0$), and this applies to all values of $n > 1$. If $n = \infty$ the further terms in the numerator of equation (5), involving higher powers of x than x^2, are absent. Therefore the plot of $x/(V/V_m)$ against x for certain values of c, starting from $x/(V/V_m) = 1/c$ when $x = 0$, has then the same gradient for small x values, whatever the n values $(n > 1)$.

Returning now to the isotherm, it can be seen that it follows that at these small values of x the curves are hyperbolæ of the same type as before; in fact the isotherm can be written in these regions for all values of $n > 1$, $V/V_m = [cx/(1 + x(c - 2)]$, the asymptote equations being $V/V_m = c/(c - 2)$ and $x = -1/(c - 2)$. If $c > 2$ there is in this region of x values a Type I isotherm (in the sense that it is concave to the x axis); if $c < 2$ there is a Type III curve in this region (convex to the x axis). If $c = 2$ the term in x in the denominator is zero and $V/V_m = 2x$ (*i.e.*, a straight line of gradient 2). It is thus clear why the approximately linear portion of the isotherm for $c = 2$ extends for some distance from the origin (see Fig. 2); this linear portion is further extended because of the incidence of the second point of inflection at $x = ca.$ 0·21 for $n = 3$. For $c = 1$ the curve is convex to the x axis at first, but later has an approximately linear region located round the point of inflection at $x = ca.$ 0·6. If c is large the approximation $V/V_m = cx/(1 + cx)$ will be satisfactory at these sufficiently low values of x.

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337. *The Structure of the Dinitrososulphite and Sulphamate Ions.*

By G. A. JEFFREY and H. P. STADLER.

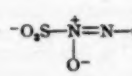
The earlier work on potassium " dinitrososulphite " $K_2SO_3{\cdot}N_2O_3$ (Cox, Jeffrey, and Stadler, *J.*, 1949, 1783) has been extended by the *X*-ray analysis of the isomorphous ammonium compound $(NH_4)_2SO_3{\cdot}N_2O_3$ with a technique leading to greater precision in the measurement of the bond lengths. These are S–O 1·44, S–N 1·79, N–N 1·33, N–O 1·28$_5$ A. Comparison with values reported for other molecules indicates that S–N is a single bond, and that N–N and N–O are multiple bonds of order 1·5 or greater. The structure of the ion is in good general agreement with the molecular-orbital calculations by Evans and Gergely, although the N–O π-bonding may have been underestimated.

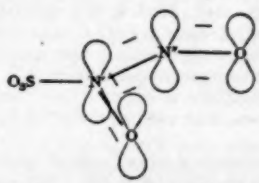
The structure of some related molecules is discussed.

The structure analysis of potassium sulphamate $KSO_3{\cdot}NH_2$ by Brown and Cox (*J.*, 1940, 1) has also been extended by the inclusion of " termination-of-series " corrections. The bond lengths S–N 1·60 and S–O 1·44 A., are not significantly different from the earlier values. The sulphamate ion is well represented by $H_2\overset{+}{N}{:}SO_3^{-}$. The significant difference between the S–N bond lengths in the two ions is ascribed to different degrees of π-bonding, and appears to be related to the ease of hydrolysis in acid solution. In the sulphonate group of both ions the S–O lengths all correspond to double bonds.

THE *X*-ray structure analysis of Pelouze's salt, $K_2SO_3N_2$ (Cox, Jeffrey, and Stadler, *Nature*, 1948, **162**, 770; *J.*, 1949, 1783), showed that the anion had a configuration and structure which, in terms of a conventional bond diagram, is best represented by (I). Of particular interest was

(I.)





(II.)

the planarity of the N_2O_3 group and the character of the N–N and N–O bonds, the length of the former corresponding to a double bond and of the latter to bond orders of about 1·2. A description of the electronic structure of the ion was given by Evans and Gergely (*Nature*, 1948, **162**, 771)

on the basis of the assumption of a molecular orbital system of π-bonding throughout the N_2O_2 group as pictorially represented in (II). Evans and Gergely's estimates of the bond orders agreed quite well with the observed bond lengths, but owing to the large experimental errors associated with the structure analysis, the agreement could only provide confirmation of the general qualitative description of the electronic structure. It seemed desirable therefore to measure the molecular dimensions as accurately as possible in order to test the theoretical treatment more critically, and if necessary to indicate the directions in which the theory might be improved to achieve a more exact description of the electron distribution in the ion.

The object of the original *X*-ray analysis was to establish the then unknown configuration of the potassium salt, and the refinements of experimental and computational techniques necessary to achieve a higher degree of accuracy in the atomic co-ordinates were not attempted. The errors associated with the original bond lengths were estimated at about $\pm 0{\cdot}06$ A. and for some bonds it appears that this was an underestimate.

The principal corrections necessary for high accuracy are (i) crystal adsorption corrections; these are important because of the high absorption coefficient of the potassium ions, but in application would involve very laborious calculations; and (ii) the " termination-of-series " corrections in the Fourier syntheses. Other recent investigations on sulphur-containing

FIG. 1.

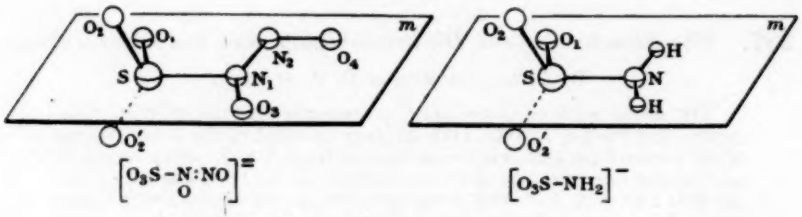
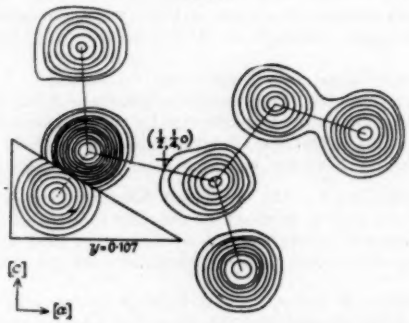


FIG. 2.



structures [*e.g.*, thiophthen (Cox, Gillot, and Jeffrey, *Acta Cryst.*, 1949, **2**, 356) and isoprene sulphone (Jeffrey, *ibid.*, 1951, **4**, 58)] showed that these corrections could lead to amendment of bond lengths by as much as 0·06 A. in certain cases.

To overcome the absorption errors, a new series of careful experimental measurements were made on the isomorphous ammonium salt, $(NH_4)_2SO_3{\cdot}N_2O_2$, with the object of obtaining as accurate and complete a set of *X*-ray intensities as possible. The known structure of the potassium salt was then used as a starting point for the more refined analysis of the ammonium salt.

The " termination-of-series " effects were corrected for by the now standard technique first suggested by Booth (*Proc. Roy. Soc.*, 1946, *A*, **188**, 77) of examining the Fourier synthesis with the calculated structure factors as coefficients; this method had already been successfully applied in the thiophthen, isoprene sulphone, and several other structure analyses.

The marked difference of the S–N bond-lengths in potassium dinitrososulphite and potassium

sulphamate $KSO_3 \cdot NH_2$ (Brown and Cox, *J.*, 1940, 1; Ketelaar and Heilmann, *Z. Krist.*, 1941, **103**, 41) which has already been remarked upon (Cox, Jeffrey, and Stadler, *loc. cit.*) was thought worthy of further study, and a refinement of the analysis of the sulphamate ion has therefore been made. No new experimental measurements have been made on this compound because the original data were recorded with Mo-K_α radiation for which the crystal absorption errors could be neglected. The termination-of-series errors, however, were likely to be as important as for the dinitrososulphite salt, and the necessary calculations to correct for these effects were carried out on Brown and Cox's original data.

The space-groups for the dinitrososulphite and sulphamate salts are *Pnma* and *Pbma*, respectively, and in both crystal structures the anions are oriented with their mirror planes of symmetry (see Fig. 1) at $y = \frac{1}{4}$. The atomic co-ordinates were therefore obtained from (i) sectional Fourier syntheses at $y = \frac{1}{4}$ with the observed and calculated structure factors as coefficients; and (ii) section and line syntheses through the oxygens symmetrically above and below the mirror planes, which were also computed for the observed and calculated structure factors. The greater part of these calculations were carried out on Hollerith computing equipment, by using methods described elsewhere (*e.g.*, Greenhalgh and Jeffrey, *Acta Cryst.*, 1950, **3**, 311; Greenhalgh, *Proc. Leeds Phil. Lit. Soc.*, 1950, in the press).

The structure analysis of the ammonium dinitrososulphite was refined directly from the co-ordinates of the potassium salt, and required three successive Fourier syntheses and sets of structure factor calculations. The final agreement index $\Sigma(|F_{obs.}| - |F_{calc.}|)/\Sigma|F_{obs.}|$ was 0·19. The electron-density contour map is shown in Fig. 2. The results of the calculations are given in Table I which refers to the numbering of the atoms given in Fig. 1.

TABLE I.

Ammonium Dinitrososulphite.—Space-group, *Pmna*, $Z = 4$; cell dimensions: $a = 7{\cdot}445 \pm 0{\cdot}003$, $b = 8{\cdot}154 \pm 0{\cdot}004$, $c = 10{\cdot}261 \pm 0{\cdot}010$ A.; $V = 622{\cdot}9$ A.^{3}; $M = 176{\cdot}16$.

Atomic co-ordinates (A.) *from the cell origin.*

Column A gives the co-ordinates from $F_{obs.}$ syntheses.
Column Δ gives the " termination-of-series " correction.
Column C gives the co-ordinates corrected for termination-of-series errors.

	X.			*Y.*			*Z.*		
Atom.	A.	Δ.	C.	A.	Δ.	C.	A.	Δ.	C
S	2·653	+ 0·001	2·654	2·038	0·000	2·038	0·085	− 0·001	0·084
N_1	4·433	− 0·022	4·411	2·038	0·000	2·038	− 0·310	+ 0·018	− 0·292
N_2	5·249	− 0·010	5·239	2·038	0·000	2·038	0·749	− 0·004	0·745
O_1	2·561	0·000	2·561	2·038	0·000	2·038	1·513	+ 0·032	1·545
O_2	2·237	− 0·027	2·210	0·871	− 0·049	0·822	− 0·517	− 0·017	− 0·534
O_3	4·760	+ 0·012	4·772	2·038	0·000	2·038	− 1·524	− 0·002	− 1·526
O_4	6·473	− 0·003	6·470	2·038	0·000	2·038	0·365	+ 0·017	0·382
NH_4	0·357	—	—	− 0·057	—	—	2·001	—	—

Atomic co-ordinates in fractions of cell dimensions.

	x.	*y.*	*z.*		*x.*	*y.*	*z.*		*x.*	*y.*	*z.*
S	0·3565	0·2500	0·0082	O_1	0·3440	0·2500	0·1506	O_2	0·6409	0·2500	0·8513
N_1	0·5925	,,	0·9715	O_3	0·2968	0·1008	0·9480	O_4	0·8692	,,	0·0373
N_2	0·7037	,,	0·0726	O_3'	0·2968	0·3992	0·9480	NH_4	0·048	0·993	0·195

Bond lengths (A.) *and valency angles.*

S–N_1	1·791	N_1–N_2	1·327	O_1–S–O_2	114·2°	S–N_1–N_2	116·5°
S–O_1	1·464	N_1–O_3	1·286	O_2–S–O_3'	116·0	S–N_1–O_3	118·4
S–O_2, S–O_3'	1·434	N_2–O_4	1·284	O_1–S–N_1	105·7	O_3–N_1–N_2	125·1
				O_3–S–N_1	102·2	N_1–N_2–O_4	112·2

For the potassium sulphamate, all Brown and Cox's experimental data were included in the calculations with the exception of the terms for three reflections, (061), (171), (544), for which the agreement between the observed and calculated structure factors was exceptionally poor. The termination-of-series corrections were therefore somewhat larger than if these terms had been included in the calculated syntheses. The results for the sulphamate structure analysis are given in Table II.

TABLE II.

Potassium Sulphamate.—Space-group, *Pbma*, $Z = 4$; cell dimensions: $a = 8{\cdot}333$, $b = 8{\cdot}302$, $c = 5{\cdot}907$ A.; $V = 408{\cdot}6$ A.^{3}; $M = 135{\cdot}18$.

Atomic co-ordinates (A) *from cell origin.*

Column references as in Table I.

Atom.	*X.* A.	*X.* Δ.	*X.* C.	*Y.* A.	*Y.* Δ.	*Y.* C.	*Z.* A.	*Z.* Δ.	*Z.* C.
S	1·136	+ 0·020	1·156	2·075	0·000	2·075	1·063	− 0·010	1·053
N	2·577	+ 0·044	2·621	2·075	0·000	2·075	1·671	+ 0·016	1·687
O_1	1·319	− 0·019	1·300	2·075	0·000	2·075	− 0·374	+ 0·004	− 0·370
O_2	0·520	− 0·019	0·501	0·816	+ 0·070	0·885	1·520	0·000	1·520
O_2'	0·520	− 0·019	0·501	3·336	− 0·070	3·266	1·520	0·000	1·520
K	2·083	—	—	0·00	—	—	3·916	—	—

Atomic co-ordinates in fractions of cell dimensions.

	x.	*y.*	*z.*		*x.*	*y.*	*z.*		*x.*	*y.*	*z.*
S	0·139	0·250	0·178	O_1	0·156	0·250	0·938	O_2'	0·060	0·394	0·260
N	0·315	0·250	0·286	O_2	0·060	0·106	0·260	K	0·250	0·000	0·663*

* Original value from Brown and Cox (*loc. cit.*).

Interatomic distances (A.) *and valency angles.*

S–N	1·60	S–O_2	1·45	O_1–S–N	108°
S–O_1	1·42			O_2–S–N	107
O_2–S–O_2'	111°				
O_1–S–O_2	112				

The Accuracy of the Results.—The standard deviations of the atomic co-ordinates were calculated from the differences between the observed and calculated structure factors, and the curvature of the atomic electron-density peaks by the formulæ derived by Cox and Cruickshank (*Acta Cryst.*, 1948, **1**, 92). For the ammonium dinitrososulphite, the standard deviations of the individual atomic co-ordinates in the x and z directions are given in Table III. The values for

TABLE III.

Standard deviations of atomic co-ordinates (A.) *for* $(NH_4)_2SO_3{\cdot}N_2O_2$.

	x.	*z.*		*x.*	*z.*		*x.*	*z.*
S	0·0035	0·0030	O_3	0·0112	0·0085	N_1	0·0129	0·0099
O_1	0·0141	0·0121	O_4	0·0137	0·0101	N_2	0·0132	0·0108
O_2	0·0141	0·0111						

the oxygen and nitrogen atoms are not significantly different; the z co-ordinates appear to be slightly more reliable than the x co-ordinates. From the root-mean-square values, the standard deviations, σ, for the bonds are

σ for S–N and S–O, 0·0124 A.; σ for N–N and N–O, 0·0168 A.

For the potassium sulphamate structure the agreement between the observed and calculated structure factors was less good. The mean standard deviation for the sulphur atom was 0·0085 A., and for the nitrogen and oxygen atoms 0·025 A. For the bond lengths the standard deviation was 0·028 A. This lower standard of accuracy, as compared with the dinitrososulphite analysis, probably reflects the greater difficulty of obtaining accurate eye-estimated intensity measurements from photographs taken with molybdenum radiation.

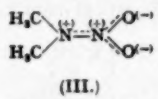
Using the significance test $P = 1 - \text{erf.}\,(\Delta/\sqrt{2}\sigma)$, where P is the probability that a difference Δ is due to random errors, we used these standard deviations to compare the various experimental and theoretical bond lengths, with the following conclusions: (*a*) The difference of 0·19 A. between the S–N bonds for the dinitrososulphite and the sulphamate ions corresponds to a P value of $< 1 \times 10^{-9}$ and is highly significant. (*b*) The difference of 0·03 between S–O_1 and S–O_2 of ammonium dinitrososulphite corresponds to $P = 0{\cdot}09$ and is probably not significant, particularly in view of the large termination-of-series corrections to the O_2 position (without which the S–O_2 distance would be 1·38 A.). (*c*) The comparison with the two sets of theoretical bond lengths (A.) obtained by Evans and Gergely (*loc. cit.*) is tabulated below:

	Calc.	Exptl.	*P.*		Calc.	Exptl.	*P.*
N–N	1·30	1·327	0·11, not significant	N–O	1·32	1·285	0·036, possibly significant
	1·29	—	0·027, possibly significant		1·33	—	0·007, significant

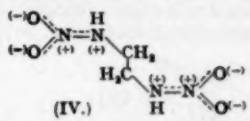
Discussion.

The Dinitrososulphite Ion.—Although the refinement of the analysis has changed the bond lengths appreciably from the values previously reported, the general description of the structure is still that approximately represented by the bond diagram (I). The S–N length of 1·79 A. must correspond very closely to that of a pure single σ-bond. There are no recorded measurements of other S–N single bonds, except in the structure of N_4S_4, for which values of 1·74 A. (Hassell and Viervoll, *Tidsskr. Kemi Berg.*, 1943, **3**, 7) and 1·62 A. (Lu and Donohue, *J. Amer. Chem. Soc.*, 1944, **66**, 818) have been reported from electron-diffraction studies; this however appears to be a cyclic molecule of unusual configuration with a non-bonded S–S distance of 2·69 A. The sum of Pauling's covalent radii (" Nature of the Chemical Bond," 1945) gives 1·74 A. for a single N–S bond, and the same value is obtained from the radii revised by Stevenson and Schomaker (*J. Amer. Chem. Soc.*, 1941, **63**, 47) using an electronegativity correction. On the other hand, analogy with the well-established C–N = 1·48 A., C–S = 1·81 A. (cf. Cox and Jeffrey, *Proc. Roy. Soc.*, in the press), and N–N = 1·48 A. suggests a value close to 1·81 A. for $\overset{+}{N}$–S.

The N–N bond length of 1·33 A. corresponds to a considerable amount of π-bonding, being much closer to the double-bond value of 1·26 A. than to the single-bond value of 1·48 A. A similar multiple N–N bonding has been found in dimethylnitramine (III), with N–N = 1·26 A.



(III.)



(IV.)

by Costain and Cox (*Nature*, 1947, **160**, 826) and 1·30 A. by Bastiansen using electron diffraction (cf. *Acta Cryst.*, 1950, **3**, 53), and in ethylenedinitramine (IV), with N–N = 1·33 A. by Llewellyn and Whitmore (*J.*, 1948, 1316).

The two N–O bonds in the dinitrososulphite ion are identical in length, within the limits of the experimental errors, at 1·28$_3$ A. This is considerably shorter than reported in the preliminary work, but longer than the N–O bond lengths found for the nitro-group and the nitrate and nitrite ions, for which the more recent experimental measurements (in A.) are given below :

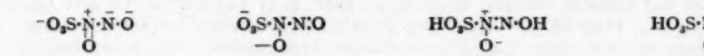
$(CH_2)_3N{\cdot}NO_2$	1·25	Costain and Cox (*loc. cit.*).
$NO_2{\cdot}C_6H_4{\cdot}NO_2$	1·21	Llewellyn (*J.*, 1947, 884).
$CH_3{\cdot}NO_2$	1·22	Rogowski (*Ber.*, 1942, **75**, 244).
$NH_4{\cdot}NO_3{\cdot}2HNO_3$	1·20 1·22 1·33	Duke and Llewellyn (*Acta Cryst.*, 1950, **3**, 305).
NO_2 in $NO_2^+NO_3^-$	1·24	Grison, Eriks, and Vries (*ibid.*, p. 190).

It corresponds to a π-bond order of 0·5, or greater if we take the N–O single-bond length to be near the value of 1·45 A. in hydroxylammonium chloride and bromide (Jerslev, *Acta Cryst.*, 1948, **1**, 21).

The N_1 bond formation is based on the trigonal hybridisation $[sp^2]^1$, $[sp^2]^1$, $[sp^2]^1$, p^2 of the valency electons with the idealised valency angles of 120°. The observed angles of $S–N_1–N_2$ = 117°, $S–N_1–O_3$ = 118°, and $O_3–N_1–N_2$ = 125° show a deviation from the trigonal symmetry which is accounted for by the strong repulsion to be expected between the negatively charged O_3 and O_4, at an equilibrium distance in the ion of 2·55 A. Similarly, the $N_1–N_2–O_4$ angle of 112° is greater than the ideal 90° for a pyramidal nitrogen, and corresponds to a hybridisation intermediate between s^2, p^1, p^1, p^1 and $[sp^2]^1$, $[sp^2]^1$, $[sp^2]^1$, p^1. Despite this difference in the two nitrogen atoms, the structure analysis shows no difference between the two N–O bond lengths. This fully justifies the assumption to that effect made in the calculations of Evans and Gergely (*loc. cit.*), whose theoretical results agree well with the more accurate bond lengths for the dinitroso-group. The comparison given above suggests that possibly the calculated N–N bond order is too great, and, of more significance, the N–O π-bonding has been underestimated. This comparison of bond lengths, however, is dependent upon the N–N and N–O bond order–length relationship, for which the direct experimental data are at present somewhat inadequate. Until this limitation has been removed, the theoretical discussion by Evans and Gergely appears to give as good a description of the electronic distribution in the dinitroso-group as can be expected.

In qualitative terms, the six π-electrons of the $N_2O_2^-$ occupy three molecular orbitals; two of these are bonding in character and extend over all four atoms, while the third is largely non-bonding, with concentrations of electron density on the oxygen atoms.

In terms of the valence-bond diagram, the structure of the ion can be described as a hybrid of (I) with (V) and (VI), (I) being the most important. The parent acid is unknown and probably unstable under all conditions. It could be formulated as (VII) or (VIII).

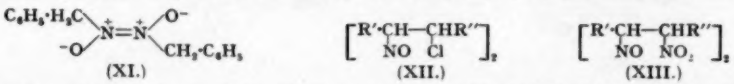


(V.) (VI.) (VII.) (VIII.)

Although we have hitherto used the long-established name " dinitrososulphite," it is not at all appropriate. By analogy of (VIII) with the amine- and hydroxylamine-sulphonic acids, the salts should be called nitrosohydroxylaminesulphonates. A structurally related compound is nitrosophenylhydroxylamine, (IX) or (X), which is a true monobasic acid forming an

(IX.) (X.)

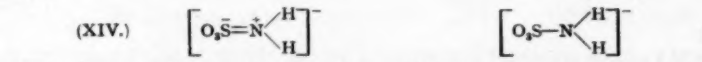
ammonium salt. A similar type of N_2O_2 group has been found in the dimer of *p*-bromonitroso-benzene (Darwin and Crowfoot Hodgkin, *Nature*, 1950, **166**, 827) and may be expected to occur in other bisnitroso-compounds, such as bis-α-nitrosobenzyl (XI) (cf. Hammick, Illingworth,



(XI.) (XII.) (XIII.)

Edwards, and Ewbank, *J.*, 1931, 3105), and the " nitrosochloride " (XII) and " nitrosite " (XIII) compounds.

The Sulphamate Ion.—Although there are some differences between the new atomic co-ordinates and those derived by Brown and Cox (*loc. cit.*), the tendency has been for the ion to shift as a whole and the new molecular dimensions are not significantly different from those previously reported. There are no other experimental measurements of S–N distances, but comparison with the dinitrososulphite value and the covalent radii sum of 1·54 A. indicates that the bond length in the sulphamate ion is close to that which may be associated with a double bond. As suggested in the earlier paper (Cox, Jeffrey, and Stadler, *loc. cit.*), the ion is better represented by (XIV) than by (XV). The nitrogen valency directions will therefore be trigonal and planar, and the hydrogen atoms will lie in the mirror plane of symmetry of the molecule (as in Fig. 1).



(XIV.) (XV.)

On the basis of N–O distances of 3·05 and 3·16 A. between adjacent sulphamate ions, Ketelaar and Heilmann (*loc. cit.*) postulate hydrogen bonding in the crystal structure. The corresponding new intermolecular distances are N . . . O_1 3·04 A., N . . . . . O_2 and N . . . . . O_2' 3·49 A.; the former is in the plane of the molecules concerned and the latter make an angle of 15° to the plane at the nitrogen end. Brown and Cox, who obtained similar interatomic distances, did not consider them short enough to imply hydrogen bridges of any appreciable strength. This view is supported by the N_2 . . . O_1 distance of 3·03 A. between adjacent ions in the dinitrososulphite structure, where there are no hydrogen atoms attached to the nitrogen. In the sulphamate structure, this distance of 3·04 A., which is admittedly somewhat shorter than is generally associated with molecular packing in crystal structures, must correspond to the effect of the electrostatic attraction between the N^+ and O^-. The existence of the similar distance in the dinitrososulphite structure suggests that the N_2 might also carry a positive charge, although the quantum-mechanical calculations and the valence-bond concept suggest a small negative charge.

The S–N *Bonds.*—The S–N bonds of the dinitrososulphite and sulphamate ions differ by 0·19 A., and comparison with the covalent radii tables shows that these bonds are close in character to the extremes of a single and a double bond, respectively. This implies that the bonding between sulphur and nitrogen always tends to have a multiple character, to a degree depending upon the nature of the adjoining atoms or groups in the molecule. In the dinitroso-

sulphite ion, however, the extensive π-bonding and electron attraction of the dinitroso-group restricts the S–N linkage almost entirely to the two σ-electrons. This may well account for the remarkable chemical properties of the dinitrososulphite ion and for the apparent incompatibility of an S–N bond with the ease of decomposition to sulphate and nitrous oxide in the presence of acids which led to the long controversy over the configuration of the salt. Potassium sulphamate does not hydrolyse readily at room temperature and requires heating in a sealed tube with hydrochloric acid at 140° to give NH_4^+ and SO_4^{--}; the free acid is also stable and can be crystallised from acid solutions of its salts, in very marked contrast to the behaviour of dinitrososulphites in the presence of acids.

In the series of amine-sulphonates, $NH_2{\cdot}SO_3^-$, $NH(SO_3)_2^{--}$, and $N(SO_3)^{\equiv}$, the rate of hydrolysis increases with the number of sulphonate groups, and further structural investigations are in progress to discover whether this can be correlated with changes in bond character. A similar progression in stability to acid hydrolysis is found in the hydroxylaminesulphonates, of which $[HO{\cdot}NH{\cdot}SO_3]^-$ is the most stable, although less so than the sulphamate ion.

The Sulphonate Group, $-SO_3^-$.—In the dinitrososulphite and sulphamate ions the bond lengths in the SO_3 group are, respectively, 1·46, 1·43, 1·43 A., and 1·42, 1·45, 1·45 A. An estimate of the probable errors in the analyses shows that no measurement is significantly different from the mean of 1·44 A. This value is consistent with other measurements of S–O bonds (in A.) given below:

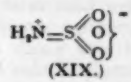
Length.	Substance.	Method.	Author.
1·43	SO_3	Elect. diffn.	Palmer (*J. Amer. Chem. Soc.*, 1938, **60**, 2360).
1·45	$SOCl_2$	,,	*Idem* (*ibid.*).
1·433	SO_3	Spect.	Dailey, Golden, and Wilson (*Physical Rev.*, 1947, **72**, 871).
1·47	$(CH_3)_2SO$	Elect. diffn.	Bastiansen and Viervoll (*Acta Chem. Scand.*, 1948, **2**, 702).
1·43	$(CH_3)_2SO_2$	,,	Rundle (see *Acta Cryst.*, 1950, **3**, 53).
1·44	$C_5H_8{\cdot}SO_2$ (*β-iso*prene sulphone)	*X*-Ray	Jeffrey (*ibid.*, 1951, **4**, 58).
1·52	Na_2SO_4-III	*X*-Ray	Frevel (*J. Chem. Physics*, 1940, **8**, 290).

The S–O distance is remarkably constant in a variety of molecules and ions; the only exception to this is the result from the modification III of anhydrous sodium sulphate, which was reported very briefly and without sufficient detail for the accuracy to be assessed. The earlier *X*-ray analyses on crystal structures containing SO_4^{--}, SO_3^{--}, $S_2O_5^{--}$, $S_2O_6^{--}$, and $S_2O_8^{--}$ report values varying from 1·39 to 1·50 A., which are conveniently tabulated by Phillips, Hunter, and Sutton (*J.*, 1945, 149), who point out that the more reliable S–O distances are very short, about 0·05 A. shorter than the Pauling covalent radii sum, and would appear to correspond to sulphur–oxygen double bonds. From a theoretical molecular-orbital treatment of S–O bonds in sulphones and sulphoxides, Moffitt (*Proc. Roy. Soc.*, 1950, *A*, **200**, 409) concludes that

(XVI.)

(XVII.)

(XVIII.)


(XIX.)

the 3*d* orbitals of the sulphur are utilised in bond hybridisation and that these molecules are best represented by (XVI) and (XVII). The calculated π-bond orders for the sulphur–oxygen bonds are about 0·9 and the atoms have formal charges in the direction $\overset{+}{S}-\overset{-}{O}$. Our results for the bond lengths in the sulphonate group suggest the analogous representation (XVIII) with bonds of similar character. The electronic distribution for the sulphamate ion is then described by (XIX), with S–O π-bond orders of about 0·9 as in the sulphones; in view of the difference of 0·16 A. between $S=\overset{-}{O}$ and $S=\overset{+}{N}$, the S–N π-bond order is probably rather less than 0·9. There will be an accumulation of negative charge towards the oxygens and away from the nitrogen in the ion, as supported by the following cation–anion interatomic distances in the crystal structure:

Cation–anion interatomic distances (in A.)

$NH_2{\cdot}SO_3K$.		$(NH_4)_2SO_3.N_2O_3$.			
K ... O_1 ..... 2·75		NH_4 ..... O_1 ..... 3·08, 3·04		NH_4 ..... O_4 ... 2·96, 3·16	
K ... O_2 ..... 2·84, 3·00		NH_4 ..... O_2 ..... 2·94, 3·05		NH_4 ..... N_1 ... 3·62, 3·74, 4·03	
K ... O_3 ..... 1·84, 3·00		NH_4 ..... O_3 ..... 2·91, 3·08		NH_4 ..... N_2 ... 3·38, 3·54, 3·86	
K ... N ..... 3·08					

EXPERIMENTAL.

Ammonium Dinitrososulphite.—The salt was prepared by a method analogous to that of Weitz and Achterberg (*Ber.*, 1933, **66**, 1718) for the potassium salt. To avoid decomposition, the crystal had to be cooled during the exposure to *X*-rays. It was enclosed in a Cellophane tube through which passed a stream of cold dry air supplied by evaporation of liquid air in a Dewar syphon.

The unit cell dimensions were measured from photographs taken by Straumanis's method and calculated for Cu-K_α 1·5411 A.

To minimise absorption errors in the intensity measurements, small, evenly developed crystals of 0·2 mm. diameter were used. Weissenberg equi-inclination photographs were taken for the layer lines 0 to 3 about [010], and 0 to 4 about [100] and [001]. In order to estimate by eye the full range of intensities, the multiple-film technique with four films interleaved with 0·001" aluminium foil was used. The comparatively large uncertainties in the high-intensity reflections were reduced by correlating them amongst themselves on photographs taken by the " double-slit Weissenberg method " (Stadler, *Acta Cryst.*, 1950, **3**, 262). After application of the usual geometrical correction factors, the correlation factors between the layer lines of the [010] and [100] which gave the best self-consistency were applied to bring all the estimated intensities on to the same relative scale. The intensities on the layer lines of the [001] were then corrected to that scale. Of the 764 possible reflexions which could be recorded with Cu-K_α radiation, 588 intensities were measured. No corrections were applied for extinction.

The authors express their gratitude to Professor E. G. Cox, for his interest and criticism, and to the University of Leeds for a senior Ellison Fellowship awarded to one of them (H. P. S.). They are also pleased to acknowledge the computational assistance given by Miss Barbara Long and Mr. D. Greenhalgh, and Mr. Grudemo during his visit from the Cement och Betong Institutt, Stockholm. Much of the experimental and computational work was done with equipment provided by the Royal Society, D.S.I.R., and Imperial Chemical Industries Limited.

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338. *Extraction of Ceric Nitrate by Solvents.*

By A. W. WYLIE.

It is shown that ceric nitrate can readily be extracted into ethyl ether if the solution is made 5—6N. in nitric acid and if peroxide-free solvent is employed. The method is convenient for separation of small quantities of pure cerium from mixtures of lanthanon nitrates. These nitrates, which are inappreciably extracted under the conditions used, act as mild " salting out " agents for ceric cerium. The complex is shown to consist of $H_2[Ce(NO_3)_6]$ or a mixture of this substance and $H[Ce(NO_3)_5(H_2O)]$. Extraction of nitric acid in various solvents has been investigated, and the results have been interpreted in terms of the structure of the solvents and the formation of oxonium nitrates. Notable extraction of cerium is found only in solvents which readily extract nitric acid from aqueous solutions. It is considered that the complex, though largely un-ionised, may be held in the solvent phase by van der Waals and oxonium-type forces.

EXTRACTION of ceric nitrate from aqueous solutions with ethyl ether was reported by Imre (*Z. anorg. Chem.*, 1927, **164**, 214) who suggested the method as suitable for purification of cerium. The extraction has been reinvestigated with mixed lanthanon nitrates, and has been found quite as convenient as classical methods for preparation of small quantities of pure cerium. Considerably greater extraction was obtained than reported by Imre, whose results were probably vitiated by reduction of cerium before analysis.

The nitric acid concentration was found to be critical for the extraction, an acidity not less than 5N. being desirable. The cerium concentration was relatively unimportant. Mixed neodymium–praseodymium nitrates in the aqueous phase have a beneficial effect on the extraction of cerium, acting as a useful salting out agent in 5N-acid at sufficiently high salt concentrations.

Both ceric nitrate and nitric acid may be rapidly and quantitatively recovered from ether by back-extraction into water. A disadvantage of the extraction procedure is the partial reduction of ceric to cerous cerium occurring when the aqueous phase is kept for a long time in bright daylight or warmed to expel ether. Ether peroxides also cause rapid reduction of

ceric cerium. The usual end product of the extraction is therefore an acid solution of ceric nitrate containing a variable proportion of cerous nitrate. Reduction of cerium in the ether phase is very slow with pure solvent, but ultimately causes separation into a cerium-free, ether–nitric acid layer, and an ether-saturated, cerous nitrate–nitric acid–water layer. Reduction in both phases is catalysed by daylight, and in the ether phase is rapid in radiation of wave-lengths between 2536 and 4046 A. As absorption in aqueous and ethereal phases above 6000 A. is small, photochemical reduction would presumably be minimised by handling solutions in red or yellow light. Such precautions, however, were ignored in the present work.

Examination of a number of other commonly available solvents of low, or negligible solubility in water, showed that either the distribution ratios under the conditions used were less favourable than with ether or the solvents were more susceptible to oxidation by ceric cerium. Although equilibrium was, unavoidably, established incompletely in these extractions, it is usually believed that equilibrium is rapidly established in the system inorganic salt–water–organic solvent–acid or other complexing agent. If it is assumed that the extraction figures given approximate to equilibrium values, the order of extraction in homologous solvents may be compared with that given for the solubility in similar solvents of thorium nitrate tetrahydrate and uranyl nitrate hexahydrate (Templeton and Hall, *J. Phys. Coll. Chem.*, 1947, **51**, 1441; Rothchild, Templeton, and Hall, *ibid.*, 1948, **52**, 1006; Yaffe, *Canadian J. Res.*, 1949, **27**, *B*, 638). In general, for homologous compounds, the extractability of cerium parallels the solubility of thorium and uranyl nitrates in decreasing with increasing molecular weight of the solvent.

Recently, Warf [*J. Amer. Chem. Soc.*, 1949, **71**, 3257; A.E.C.D. (U.S.A.) No. 2524, 1949] proposed tri-*n*-butyl phosphate for extraction of ceric nitrate. Whereas ethyl ether extracts less than 0·3% of La_2O_3, from a 5N-nitric acid solution of lanthanum nitrate containing 65 g. of La_2O_3 per l., it was stated that butyl phosphate extracts from nitrate solutions 4—7% of La_2O_3 and up to 15% of Pr_2O_3. Ether is therefore to be preferred for separation of ceric cerium from other lanthanons, in spite of the greater stability claimed for butyl phosphate. Other disadvantages of butyl phosphate are the necessity for reduction of cerium before back-extraction into water, and the reported necessity for an additional treatment to overcome phosphate contamination of the products.

Nature of the Extracted Ceric Complex.—Negligible extraction of cerium from solutions of ceric nitrate, either weakly acid with nitric acid or 5N. with respect to ammonium nitrate, emphasises the important rôle of nitric acid in the extraction with ethyl ether and other solvents. The system differs, in fact, in a number of respects from the uranyl nitrate system which has been extensively studied in recent years.

Evidence that acidified ceric nitrate solutions contain an anionic complex has been briefly reviewed by Yost, Russell, and Garner ("The Rare-Earth Elements and their Compounds," John Wiley and Sons, N.Y., 1947, p. 61), and the existence of nitratocerate anions may be accepted therein at higher acid concentrations. According to Smith ("Cerate Oxidimetry," G. F. Smith Chemical Co., Columbus, Ohio, 1942) a 0·1M-solution of potassium hexanitratocerate in water has a pH of 1, suggesting hydrolysis according to the equation:

$$[Ce(NO_3)_6]^{--} + H_2O \rightleftarrows [Ce(OH)(NO_3)_5]^{--} + H^+ + NO_3^- \quad . \quad . \quad (i)$$

Hydrolysis of the ceric ion has been investigated by Sherrill, King, and Spooner (*J. Amer. Chem. Soc.*, 1943, **65**, 170) who postulated an equilibrium in perchlorate solution between the ions $Ce(OH)^{3+}$ and $Ce(OH)_2^{2+}$. Kraus, Holmberg, and Nelson (Amer. Chem. Soc., Abstract of 114th Meeting, 1948) concluded that cations $Ce(OH)_n^{(4-n)+}$ with $n = 1{\cdot}5$ at pH 2·3 were present in perchlorate solutions of ammonium hexanitratocerate. Since ion-migration experiments indicate the existence of anionic complexes only at high nitric acid concentrations, it may be supposed that cations of the type $Ce(OH)_n(NO_3)_m^{(4-n-m)+}$ or $Ce(NO_3)_m^{(4-m)+}$ are first formed at low or intermediate acidities in nitrate solutions of ceric cerium and that conversion of these ions into anionic complexes takes place at higher acidities, corresponding to an increase in $n + m$. The nitrate groups presumably occupy positions in the co-ordination sphere of cerium which in the partly hydrolysed ion were occupied by (H_2O) or (OH) groups. Similar types of complex ions have been noted recently for other quadrivalent ions. For instance, Connick and McVey (*J. Amer. Chem. Soc.*, 1949, **71**, 3182) attribute to n a value of between 0 and 1 for the zirconium ion $Zr(OH)_n^{(4-n)+}$ in 2M-perchloric acid. At this acidity in nitrate solution the ion $Zr(NO_3)^{3+}$ was postulated. An ion $Th(NO_3)^{3+}$ has been identified for thorium in nitric acid–perchloric acid media by Day and Stoughton (A.E.C.D. 2756, 1949). At acidities below

4·6M., Hindman ("The Transuranic Elements," Ed. by Seaborg, Katz, and Manning, Part I, p. 388) identified the ion $Pu(NO_3)^{3+}$ as the principal complex ion of plutonium(IV) in nitrate solutions; at higher acidities the ion $Pu(NO_3)_6^{2-}$ was present.

Extraction of ceric cerium is therefore possible through reversal of changes such as that represented in equation (i), resulting in the formation of a nitratoceric acid which is soluble in organic solvents containing nitric acid. Partly hydrolysed complex anions, such as $[Ce(OH)(NO_3)_5]^{1-}$, presumably fail to pass into the solvent because of the greater affinity of the hydroxyl group for the aqueous phase. More extensive hydrolysis may be presumed to result in the formation of ions such as $[Ce(OH)(H_2O)_5]^{3+}$ or $[Ce(OH)_2(H_2O)_4]^{2+}$.

The discussion has so far assumed a value of 6 for the co-ordination number of cerium. Although this is a likely value for cerium in crystalline ammonium hexanitratocerate and analogous salts, more definite evidence for the value in solution was obtained by calculating the difference between the quantity of nitric acid extracted by ether under similar conditions from a given volume of nitric acid solution both in the presence and in the absence of ammonium hexanitratocerate:

Initial acidity, N.	1·0	2·0	3·0	4·0	5·0	6·0	7·0	8·0	9·0
Mols. of HNO_3 extracted per mol. of CeO_2 at initial concentration of 39 g. of CeO_2 per l.	27	16	2·7	2·2	1·6	1·6	1·4	1·4	1·0

Chiefly because the amount of nitric acid co-extracted with the cerium complex was small, results of high accuracy were not obtained. However, within the range of initial acidities 4—9N., each molecule of ceric nitrate appears to co-extract between one and two molecules of nitric acid; $H_2[Ce(NO_3)_6]$ may therefore be present, though not as the sole complex. The aquo-complex $H[Ce(NO_3)_5(H_2O)]$ may also be present, since experiment shows that additional water, some of which may be constitutional, is brought into the ether phase by solution of the cerium complex. At acidities below 3·0N., it is assumed that ceric nitrate in the aqueous phase exerts a strong "salting-out" effect on extraction of nitric acid.

The absorption spectrum of solutions containing ceric cerium shows only the well-defined edge of a broad absorption band. The band edge shifts according to the acidity and cerium concentration from approximately 300 mμ. at low concentrations, where it overlaps an absorption band of the nitrate ion, to beyond 550 mμ. at higher concentrations. Although limited information is available from the spectrum, the absence of further shift in the absorption band above an acidity of approximately 5—7N. for the cerate concentrations given suggests that a stable complex has been produced which is not changed by further addition of acid.

The effect of "salting-out" reagents on extraction of cerium is presumed not to alter conclusions already drawn as to the nature of the extracted complex. Although no comprehensive investigation of the influence of such reagents was made, it was shown that extraction of ceric cerium into ethyl ether from a 5N-nitric acid solution of ammonium hexanitratocerate containing 39·2 g. of CeO_2 per l. was only slightly affected by additions of ammonium nitrate or "didymium" nitrate up to concentrations of 1·4 and 0·5M., respectively. By doubling the cerium concentration in 5N-nitric acid it was shown, however, that 0·76M-"didymium" nitrate caused a significant increase in the quantity of extractable cerium. High concentrations of ammonium nitrate produced a similar effect but eventually caused the separation of solid ammonium hexanitratocerate.

The Rôle of the Solvent in Extraction of Nitric Acid and the Ceric Complex.—Under the conditions used nitric acid takes with it into the solvent phase 0·4 mol. of water from a solution initially 5N. with respect to nitric acid, the resulting electrically conducting solution presumably containing nitrate ion and the oxonium ions H_3O^+ and Et_2OH^+.

Table III shows the variation in extractability of nitric acid for some ethers and ketones. With the *n*-alkyl compounds the efficiency of extraction at acidities up to 7N. lies in the order: Et>Pr>Bu>Am, resembling that found by Gordy and Stanford (*J. Chem. Physics*, 1940, **8**, 140) for the proton affinity of a number of ethers. Virtually no extraction was obtained in solvents such as chloroform, benzene, carbon tetrachloride, or light petroleum, which contain no donor oxygen atoms. There is some evidence, then, that the proton affinity of ethers and ketones is a factor influencing their extractive ability for nitric acid, oxonium-type compounds being formed in each instance. If this premise be accepted, a useful correlation between extractive power and the structure of the solvent may be derived in terms of current electronic theories of organic reactions. For example, solvents such as anisole which contain groupings which withdraw electrons from the donor oxygen atom have low extractive power for nitric

acid. Conversely, others such as acetophenone or mesityl oxide, where the electron displacement is presumably towards the donor oxygen, have a relatively high extractive power. The donor properties of the oxygen atom appear to be strongly influenced by steric effects.

Extraction of the cerium complex with alkyl ethers is seen from Tables I and III to decrease more rapidly than that of nitric acid as the number of carbon atoms in the ether molecule is increased. In general, only those solvents which extract a substantial portion of nitric acid cause notable extraction of cerium. In all cases considerable excess of nitric acid over that associated with ceric nitrate in the cerium complex is present, suggesting ready decomposition of the complex in the absence of excess of acid. In this respect, the behaviour of the complex in ether appears to be essentially the same as in water. The organic layer may contain ethoxonium or other organic oxonium cations in addition to the ions present in water. Alternatively, some form of hydrogen bonding between the solvent oxygen and the cerate group may be involved.

In so far as the proton affinity of the solvent influences the extractability of nitric acid, high acid extraction and high cerium extraction are best obtained in solvents with sterically unhindered ether and ketonic groupings which are not subject to deactivation by other groups in the molecule. In order to be suitable, a solvent should be sparingly soluble in water and reasonably resistant to oxidation by ceric cerium. The choice of solvents is thus even more restricted with cerium than with other elements. For this reason ethyl ether, which fulfils the requirements better than other solvents investigated, was the only solvent used for separation of cerium from tervalent lanthanons, but there is no reason to suppose that a more suitable solvent could not be found. Alternatively, the value of ether might be noticeably enhanced by a more extended study of the effect of " salting-out " reagents on extraction of cerium.

Experimental.

Extraction of Cerium from Ammonium Hexanitratocerate with Ethyl Ether.—5 G. of the pure dry salt, dissolved in 40 ml. of nitric acid of various concentrations (initial CeO_2 concentration, 39 g./l.) were shaken at 20° with 40 ml. of peroxide-free " AnalaR " ether.† After 3 mins., the layers were separated and the ether extract was shaken with an equal volume of water. The layers were separated and the procedure repeated until the aqueous layer was neutral to litmus paper. Ether was expelled from the combined water layers by bubbling air through the solutions at 50°, and ceric cerium was reduced by dropwise addition of pure hydrogen peroxide. Satisfactory material balances were obtained by precipitating the cerium from each phase as oxalate, before ignition, and by titrating the free acid from each phase with standard sodium hydroxide. Bromophenol-blue was used as indicator. Results of duplicate extractions agreed to within ±1%. In calculating the results allowance was made for acid liberated by the action of hydrogen peroxide on the ceric salt :

Initial acidity	0	1·0	2·0	3·0	4·0	5·0	6·0	7·0	8·0	9·0
Extraction of CeO_2, %	nil	1·1	4·5	39	69	88	93	93	94	94
Extraction of HNO_3, %	—	15	23	31	36	40	44	45	49	53

At a constant initial acidity of 5·0N., the extraction varied with initial cerium concentration as follows

Concentration of CeO_2, g./l.	8·0	39	78
Extraction, %	88	88	76

Effect of " Salting-out" Reagents on Extraction of Cerium.—Conditions were the same as those used previously, the initial concentration of nitric acid being 5N. " Didymium " nitrate (Nd_2O_3 : Pr_2O_3 = approx. 3·5 : 1) was analysed for total lanthanon oxide. Negligible amounts of neodymium or praseodymium entered the ether phase :

" Di_2O_3," g. per 40 ml. acid	0·93	1·86 *	2·79
Extraction of CeO_2, %	87	89	91
Extraction of HNO_3, %	42	44	45

* " Di_2O_3 "/CeO_2 as in monazite.

The effect of high " didymium " nitrate concentration on extraction of cerium was investigated by mixing 10 g. of ammonium hexanitratocerate, 40 ml. of 5N-nitric acid, and 12·5 g. of the nitrate (4·8 g. of " Di_2O_3 "). Extractions obtained were : CeO_2, 85; HNO_3, 52%. In the absence of " didymium " nitrate corresponding extractions were : CeO_2, 76; HNO_3, 50%. When ammonium nitrate was substituted for " didymium " nitrate the following results were obtained :

NH_4NO_3, g. per 40 ml. acid *	1·48	2·96	4·44
Extraction of CeO_2, %	88	87	86
Extraction of HNO_3, %	41	42	42

* Exclusive of NH_4NO_3 present in ceric salt.

† Commercial grades of solvent caused partial dissolution of the dry salt and reduction to cerous compounds. Pure dry ether neither reduced nor dissolved ammonium hexanitratocerate.

The effect of high ammonium nitrate concentration was investigated by mixing 10 g. of ammonium hexanitratocerate, 40 ml. of 5N-acid, and just sufficient ammonium nitrate (38 g.) to prevent precipitation of the cerium salt. An aliquot of this solution was extracted as before. Initial concentrations were: CeO_2, 29 g./l.; HNO_3, 3·95N. The extractions obtained were: CeO_2, 80; HNO_3, 55%.

Extraction of Nitric Acid with Ethyl Ether.—When pure nitric acid solutions of different concentrations were extracted under the same conditions as used for extraction of cerium, the following results were obtained:

Initial acidity, N.	1·0	2·0	3·5	5·0	6·0	7·0	8·0	9·0	10·0
Extraction, %	7·0	13	25	35	41	46	48	52	55

When the aqueous layers from the first extraction were re-extracted for 3 mins. with 40 ml. of fresh ether, the total (two-stage) extraction of acid was as follows:

Initial acidity, N.	5·0	6·0
Total acid recovery, %	54	57

Effect of "Salting-out" Reagents on Extraction of Nitric Acid.—By procedures already described, the following results were obtained with pure nitric acid containing 4·7 g. of "didymium" nitrate (1·86 g. of "Di_2O_3") per 40 ml. of acid. Shaking time was 3 mins. and only one extraction was given:

Initial acidity, N.	2·0	3·5	6·0	8·0
Extraction, %	17	27·5	43	50

With 1·35 g. of ammonium nitrate per 40 ml. of acid, the results were:

Initial acidity, N.	2·0	4·0	6·0	8·0
Extraction, %	14	28	40	61

Reduction of Ceric Complex in Aqueous and Solvent Phases.—An ether extract and a residual aqueous layer obtained by shaking equal volumes of peroxide-free ether and a 5N-nitric acid solution containing 39 g. of CeO_2 per l. were examined. The initial concentrations were: ether layer, 27 g. of CeO_2 per l., 3·3N-HNO_3; aqueous layer, 4·4 g. of CeO_2 per l., 2·4N-HNO_3. Aliquots from each layer were withdrawn at intervals and shaken with 100 ml. of 3% sulphuric acid before titration with standard ferrous ammonium sulphate solution. After 3 hrs. at 20° in diffused daylight no reduction of cerium could be detected in the ethereal layer. Less than 1% of the cerium was reduced in the aqueous layer. On warming the aqueous layer to 60° to expel ether, reduction of cerium occurred. Poorly reproducible analytical results were obtained but the figures suggested that approximately half of the cerium present was reduced after 1 hr. Mainly because of the lower acid concentration, cerium in the solution obtained by back-extracting from the ethereal layer into water was reduced to the extent of only 10—20% after 1 hr. at 60°. If the ether contained much peroxide, reduction in the aqueous layer was rapid at 20° and almost immediate at 60°. Reduction in the ethereal layer, however, was usually less than 3% after 1 hr. at 20°. Irrespective of the presence of peroxides, reduction in both phases was catalysed by sunlight, and was rapid in ultra-violet light of wave-lengths between 2536 and 4046 A. As with ethyl ether, reduction of cerium in the solvent phase of tetrahydropyran at 20° was negligible in diffused daylight; reduction in the aqueous layer, however, was almost immediate at 20°.

Separation of Ceric Cerium from Tervalent Lanthanons.—Mixed nitrates, containing ceric nitrate, were conveniently prepared by dissolving finely divided hydroxides in 66% nitric acid to give a 6N-nitric acid solution containing approximately 107 g. of CeO_2 per l. After 3 mins.' shaking with an equal volume of ether and separation, 93% of the cerium and 76% of the free acid entered the solvent phase. Re-acidification of the aqueous layer to restore the acidity from 2·4 to 6·0N., followed by a second extraction, caused 99% of the total cerium and 84% of the total nitric acid to enter the ether layer.

The lanthanon hydroxides for the above preparation were prepared by boiling the mixed double sulphates with sodium hydroxide and drying the filtered product in an oven at 120° until 99% or more of the cerium was converted into the ceric state. To prevent formation of emulsions, preparations contaminated with finely divided silica were avoided. Thorium was removed beforehand as it is partly extracted with cerium.

The ethereal extracts were conveniently purified by shaking with fresh 6N-nitric acid, impurities present then entering the aqueous phase. Some loss of cerium necessarily resulted from this procedure.

Extraction of Tervalent Lanthanons.—Cerous nitrate and lanthanum nitrate solutions containing 65 g. of oxides per l. severally were extracted once with an equal volume of ether at 20°. At a nitric acid concentration of 5N., the extraction of lanthanon oxides was less than 0·3%.

Spectrophotometric Examinations.—The neodymium and praseodymium contents of the extracted cerium were determined photometrically (Wylie, *J. Soc. Chem. Ind.*, 1950, **69**, 143), a Beckman quartz-prism spectrophotometer being used. After a single extraction the lanthanon contents (in terms of oxides) ranged from: Nd_2O_3, 0·25—0·87%; Pr_2O_3, 0·13—0·30%. After purification as described, bands due to neodymium and praseodymium could not be detected in 4-cm. thicknesses of solutions containing 100 g. of CeO_2 per l. Transmittance curves for various solutions containing ceric cerium and nitric acid were obtained on the same instrument, 1-cm. quartz cells being used. Nitric acid solutions in ether were made by extracting aqueous nitric acid solutions of appropriate concentration.

Four series of ceric solutions were examined in which separately (*a*) the cerate salt concentration in water was increased from 0·019 to 19·5 g./l.; (*b*) the nitric acid concentration was increased at constant ammonium nitratocerate concentrations of 0·1 and 4·1 g. per 100 ml. of solution; (*c*) the cerate salt concentration in 5N-nitric acid was increased over a similar range; (*d*) an extract was prepared by shaking

5N-acid solutions of the cerate with ether. Concentrations in the ethereal layer in (*d*) were CeO_2, 32 g./l., nitric acid, 1·7N., and in the aqueous layer, CeO_2, 4·5 g./l., nitric acid, 3·2N. Increasing cerate concentrations in water (*a*) or nitric acid (*c*) caused a progressive shift of the band edge towards longer wave-lengths. Addition of nitric acid at constant cerate concentration (*b*) caused the band edge to move to longer wave-lengths as the acidity increased; no further shift of the band edge, however, occurred in the more dilute cerate solution above an acidity of 5N. With the more concentrated cerate solution no further shift occurred above an acidity of 7N. In case (*d*), the presence of ether caused the band edge to shift to wave-lengths longer than observed with equal concentrations of cerium in aqueous ether-free nitric acid of the same acidity.

Determination of Water co-extracted with Cerium Complex.—Water in ethereal extracts was determined by Zerewitinoff's method, using methylmagnesium iodide reagent dissolved in redistilled anisole. Benzoic acid was used to calibrate the apparatus. Measurements at 20° were made of the volume of methane evolved from: (*a*) the ethereal cerium extract obtained from 40 ml. of a 5N-nitric acid solution which contained in addition 5 g. of ammonium hexanitratocerate; (*b*) the ethereal extract obtained from 40 ml. of 5N-nitric acid alone. The shaking time in all experiments was 3 mins., 5 mins., being allowed for separation of the phases. After separation, the ether layers were centrifuged to remove microscopic droplets of aqueous phase.

Since the Grignard reagent gave poorly reproducible results in the absence of free acid, the quantity of water dissolved by ether alone under the conditions outlined was measured by titration with the Karl Fischer reagent, which was standardised by direct titration of water weighed from a micro-pycnometer, the end-point being detected potentiometrically. The reagent was found to reduce nitric acid present in ethereal extracts. The water contents of the ethereal layers were: (*a*) 1·1 g. per 44 ml.; (*b*) 0·83 g. per 39 ml. The molecular ratio CeO_2 : total HNO_3 : total H_2O in (*a*) was 1 : 10·2 : 7·4; in (*b*) the ratio HNO_3 : total H_2O was 10 : 6·1. The molecular ratio of CeO_2 carried into ether layer to H_2O carried into the ether by the cerium complex only was 1 : 1·80. The solubility of water in ether under the conditions given was 0·72 g./100 ml. or 1·0 g./100 g. of solution.

Extraction of Ceric Cerium with Other Solvents.—3N-, 5N-, and 7N-Nitric acid solutions of ammonium hexanitratocerate containing 39·2 g. of CeO_2 per l. were vigorously shaken for 3 mins. at 20° with various solvents to determine the extraction of cerium. Reagent-grade solvents were purified by distillation.

TABLE I.

Extraction (%) of ceric cerium and nitric acid by various ethers.

Ether.	3·1N-HNO_3.		5·0N-HNO_3.		7·0N-HNO_3.	
	CeO_2.	HNO_3.	CeO_2.	HNO_3.	CeO_2.	HNO_3.
n-Ethyl	39	31	88	40	93	45
n-Propyl	*	*	25	*	*	*
n-Butyl	*	*	<1	13	2	21
n-Amyl	<1	4·1	<1	9	<1	15·6
*iso*Propyl	1	19	19	31	51	39
Dibenzyl †	<1	4·0	1	5·0	1·4	11

* Signifies not determined.

† Some uncertainty as to the significance of very low extractions was caused by the slow rate of settling of minute droplets of aqueous solution from the solvent layer of this substance.

Only ethers free from peroxides were employed. Peroxidised samples were first shaken with acid ferrous sulphate, separated, and dried (K_2CO_3) before distillation. Results for ethers are given in Table I, those for ethyl ether being included for comparison.

Anisole and phenetole, which did not appear to extract cerium, formed dark oxidation products. Tetrahydromethylfuran caused rapid reduction to cerous compounds even in 1N-acid. Although

TABLE II.

Extraction (%) of ceric cerium and nitric acid by various ketones.

Ketone.	3·0N-HNO_3.		5·0N-HNO_3.		7·0N-HNO_3.	
	CeO_2.	HNO_3.	CeO_2.	HNO_3.	CeO_2.	HNO_3.
tert.-Butyl methyl	—	—	73	34	—	—
Benzyl methyl	—	—	<2 *	—	—	—
Dibenzyl	<1 *	<1 *	<2 *	7·0	6·5	19
Acetophenone	60	22	71	28	71	34
Propiophenone	—	—	41	23	—	—

* See second footnote, Table I.

tetrahydropyran and di-2-butoxyethyl ether gave high extractions of cerium, variable results were obtained owing to very rapid reduction of cerium remaining in the aqueous phase. Tetrahydropyran (dried over sodium) was the only ether which dissolved solid cerate or extracted cerium from unacidified solutions. Pale yellow solutions formed in each instance. Results for some ketones are given in Table II. Slowly separating emulsions formed with the last four solvents, particularly during back-extraction of cerium into water. Only the water layer was analysed in such cases. Di*iso*propyl ketone, amyl methyl ketone, hexyl methyl ketone, *cyclo*hexanone, and mesityl oxide caused immediate reduction to cerous compounds. Diethyl ketone, methyl propyl ketone and *iso*butyl methyl ketone all extracted

cerium, but rapid reduction in the aqueous phases, and slower reduction in the solvent phases, prevented useful results from being obtained. Of these three ketones, the last was the most stable. Only acetone, methyl propyl ketone, *iso*butyl methyl, and *tert.*-butyl methyl ketones dissolved dry ammonium hexanitratocerate.

Aliphatic alcohols dissolved ammonium hexanitratocerate freely, higher alcohols causing extraction of cerium from 0·2M-aqueous solutions of the salt. Visual observation showed the intensity of the red-brown colour of cerate–alcohol extracts to decrease with increasing molecular weight of the alcohol. Rapid reduction of cerium in 5N-acid occurred with commercial hexyl and octyl alcohols and with *cyclo*hexanol. With *n*-amyl alcohol, extractions from 5N-nitric acid solutions containing 39·2 g. of CeO_2 per l. were: CeO_2, 13%; HNO_3, 44%. In the absence of acid, extraction of CeO_2 was 12%, but instability of the solvent influenced the results obtained.

TABLE III.

Extraction of nitric acid in various solvents.

Solvent.	Extraction, %.* 3N.	5N.	7N.	Solvent.	Extraction, %.* 3N.	5N.	7N.
Diethyl ether	21	36	47	Methyl *n*-propyl ketone	31	39	50
Di-*n*-propyl ether	—	15	—	*iso*Butyl methyl ketone	25	33	39
Di*iso*propyl ether	14	26	36	*tert.*-Butyl methyl ketone	22	28	38
Di-*n*-butyl ether	3·6	11	19	*n*-Amyl methyl ketone	20	28	35
Di-*n*-amyl ether	2·5	7·1	14	*n*-Hexyl methyl ketone	17	25	30
2 : 2′-Dichlorodiethyl ether	1·9	4·2	9·8	Methyl *n*-nonyl ketone	10	16	21
Tetrahydropyran	39	51	62	Diethyl ketone	24	34	41
Di-2-butoxyethyl ether	29	39	45	Di*iso*propyl ketone	17	25	30
Anisole	—	<2	10	Acetophenone	18	28	35
Phenetole	—	<1	2·6	Propiophenone	—	15	—
Dibenzyl ether	—	5·3	—	Mesityl oxide	34	42	51
				Dibenzyl ketone	—	7·0	—
				Benzyl methyl ketone	—	23	—

* With 1N-nitric acid extractions with tetrahydromethylfuran and 2 : 5-dimethyldioxan were 24% and 4%, respectively.

Extraction of Nitric Acid with Organic Solvents.—5N-Nitric acid was shaken for 5 mins. at 21° with various solvents to ascertain the extent of nitric acid extraction in the absence of cerium. *cyclo*Hexanone, 2 : 5-dimethyldioxan, and tetrahydromethylfuran gave single-phase solutions. Results with other solvents are shown in Table III.

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339. *Deoxy-sugars. Part XIX. The Conversion of* D-*Arabinose into* 3-*Deoxy*-D-*xylose Derivatives.*

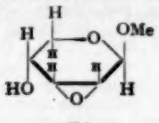
By R. ALLERTON and W. G. OVEREND.

Cleavage of the anhydro-ring in β-methyl-2 : 3-anhydro-D-riboside with hydrochloric acid results in the formation predominantly of β-methyl-3-chloro-3-deoxy-D-xyloside. Scission of the anhydro-ring with lithium aluminium hydride gives mainly β-methyl-3-deoxy-D-xyloside. Fresh evidence is forwarded to support the structures already assigned to the methylglycosides of 2-deoxy-D-ribose (cf. Stacey *et al.*, *J.*, 1949, 2836).

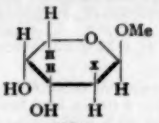
IN attempts to prepare 2-deoxyribose in improved yield, Kent, Stacey, and Wiggins (*J.*, 1949, 1232) showed that β-methyl-2 : 3-anhydro-D-riboside (I) when treated with hydrobromic acid yielded mainly β-methyl-3-bromo-3-deoxy-D-xyloside. This work has now been extended and the methylanhydroriboside has been treated with hydrochloric acid to determine whether the halogeno-derivative of arabinose (II; X = Cl) could be obtained in larger amount. The results were simliar to those obtained when using hydrobromic acid, the predominant product being β-methyl-3-chloro-3-deoxy-D-xyloside (III; X = Cl).

β-Methyl-2 : 3-anhydro-D-riboside (I) (cf. Honeyman, *J.*, 1946, 990) was prepared by the method described by Kent *et al.* (*loc. cit.*) and was characterized as its crystalline 4-acetyl-,

4-toluene-*p*-sulphonyl-, 4-benzoyl-, and 4-*p*-nitrobenzoyl derivatives. Treatment of the anhydroriboside with hydrochloric acid in acetone afforded a syrupy mixture of β-methyl-2-chloro-2-deoxy-D-arabinoside (II; X = Cl) and β-methyl-3-chloro-3-deoxy-D-xyloside (III; X = Cl). When this mixture reacted with lead tetra-acetate under Hockett and McClenahan's conditions (*J. Amer. Chem Soc.*, 1939, **61**, 1667) the uptake of the oxidant indicated the presence



(I.)



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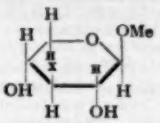

(III.)

of 18·4% of (II; X = Cl) in the mixture but, in view of the subsequent difficulties encountered in separation, this figure is considered to be high owing to some over-oxidation. The crude syrupy mixture of chloro-derivatives was hydrolysed with N-hydrochloric acid and the product examined by the chromatographic technique (see Experimental section). The chromatogram indicated that the product was predominantly derived from (III; X = Cl) and only faint indications of a derivative of (II; X = Cl) were obtained. Separation by means of the *iso*propylidene derivatives (cf. Kent *et al.*, *loc. cit.*, for separation of the corresponding bromo-derivatives) was unsuccessfully attempted but β-methyl-3-chloro-3-deoxy-D-xyloside was obtained pure.

As in the examples earlier investigated the predominant isomer was the xylose derivative, so that this method was of no value for the preparation of intermediates suitable for conversion into 2-deoxyribose derivatives. Consequently the method recently reported by Prins (*J. Amer. Chem. Soc.*, 1948, **70**, 3955) whereby 2 : 3-anhydro-rings were cleaved by lithium aluminium hydride was examined. By this method β-methyl-2 : 3-anhydro-D-riboside (I) gave a syrup which gave a positive Dische diphenylamine test (*Mikrochemie*, 1930, **8**, 4), indicating the probable presence of a derivative of 2-deoxy-D-ribose. On treatment with lead tetra-acetate, the uptake of oxidant indicated the presence of 14% of β-methyl-2-deoxy-D-riboside (II; X = H) (cf. Todd and Mukherjee, *J.*, 1947, 969), the other compound in the product being β-methyl-3-deoxy-D-xyloside (III; X = H). Attempts to separate these components as crystalline derivatives yielded only compounds derived from 3-deoxy-D-xylose, *e.g.*, 2 : 4-ditoluene-*p*-sulphonyl β-methyl-3-deoxy-D-xyloside and, after acidic hydrolysis, etc., 3-deoxy-D-xylose anilide and 3-deoxy-D-xylitol tetrabenzoate (Kent *et al.*, *loc. cit.*).

The syrupy reaction product from the ring scission was hydrolysed with N-hydrochloric acid at 100° and also at room temperature and then examined on a paper chromatogram together with authentic 2-deoxy-D-ribose and 3-deoxy-D-xylose as reference compounds. After being sprayed with aniline hydrogen phthalate and heated at 80—100° for 5 minutes, the chromatogram indicated the presence of only 3-deoxy-D-xylose. However no anomaly existed between this result and that obtained from the lead tetra-acetate oxidation since control experiments showed that the treatment required to hydrolyse β-methyl-3-deoxy-D-xyloside (III; X = H) resulted in the decomposition of the corresponding labile methylglycoside of 2-deoxy-D-ribose (II; X = H) (Deriaz, Overend, Stacey, and Wiggins, *J.*, 1949, 2836).

During this work several new derivatives of 2-deoxy-D-ribose were synthesised for comparison purposes, *e.g.*, 3 : 4-ditoluene-*p*-sulphonyl β-methyl-2-deoxy-D-ribopyranoside and 3 : 5-ditoluene-*p*-sulphonyl αβ-methyl-2-deoxy-D-ribofuranoside. The former derivative underwent no reaction when heated under anhydrous conditions with sodium iodide in acetone whereas under the same conditions the latter afforded one mol. of sodium toluene-*p*-sulphonate, thereby indicating the presence of one toluene-*p*-sulphonyloxy-group formed by esterification of a primary hydroxyl group. β-Methyl-2-deoxy-D-ribopyranoside formed a mono*iso*propylidene derivative whereas no reaction occurred with αβ-methyl-2-deoxy-D-ribofuranoside. These experiments extend and confirm the evidence put forward for the assignment of the structures to the methylglycosides of 2-deoxy-D-ribose (Deriaz *et al.*, *loc. cit.*) 2-Deoxy-D-ribose was shown to form a crystalline triacetate, tribenzoate, and *p*-nitrophenylhydrazone.

Experimental.

3 : 4-*Di*-p-*nitrobenzoyl* 2-*Toluene*-p-*sulphonyl* β-*Methyl*-D-*arabinoside*.—This was prepared by the standard method from 2-toluene-*p*-sulphonyl β-methyl-D-arabinoside and had m. p. 145—148° and $[\alpha]_D^{22}$ −207° (*c*, 0·21 in chloroform) (Found: C, 52·7; H, 3·8; N, 4·5. $C_{27}H_{24}O_{13}N_2S$ requires C, 52·6; H, 3·9; N, 4·5%).

β-Methyl-2 : 3-anhydro-D-riboside.—The anhydro-derivative was prepared both from 2-toluene-*p*-sulphonyl and from 2-methanesulphonyl β-methyl-D-arabinoside by the method described by Kent, Stacey, and Wiggins (*J.*, 1949, 1232). It was obtained as colourless needles, m. p. 52—53°, $[\alpha]_D^{18}$ −49·2°, −48·4° (*c*, 1·38, 0·43 in chloroform) (Found: OMe, 21·3. Calc. for $C_6H_{10}O_4$: OMe, 21·2%). Kent, Stacey, and Wiggins (*loc. cit.*) give m. p. 46° and $[\alpha]_D^{22}$ −35·8° in chloroform. This compound readily afforded *4-acetyl* {m. p. 73°, $[\alpha]_D^{23}$ +22·4° (*c*, 0·45 in chloroform) (Found: C, 51·0; H, 6·5. $C_8H_{12}O_5$ requires C, 51·0; H, 6·4%)}, *4-toluene-p-sulphonyl* {m. p. 89°, $[\alpha]_D^{20}$ −25·5° (*c*, 0·48 in chloroform) (Found: C, 51·9; H, 5·2. $C_{13}H_{16}O_6S$ requires C, 52·0; H, 5·3%)}, *4-benzoyl* {m. p. 106—106·5°, $[\alpha]_D^{18}$ +25·4° (*c*, 0·47 in chloroform) (Found: C, 62·4; H, 5·4. $C_{13}H_{14}O_5$ requires C, 62·4; H, 5·6%)}, and *4-p-nitrobenzoyl* {m. p. 159—160°, $[\alpha]_D^{24}$ +24·6° (*c*, 0·33 in chloroform) (Found: C, 53·0; H, 4·3. $C_{13}H_{13}O_7N$ requires C, 52·9; H, 4·4%)} derivatives.

Treatment of β-Methyl-2 : 3-anhydro-D-riboside with Hydrochloric Acid.—β-Methyl-2 : 3-anhydro-D-riboside (1·02 g.) was boiled under reflux for 4 hours with acetone (150 c.c.) containing 5N-hydrochloric acid (5 c.c.). The solution was neutralised with lead carbonate, then filtered, and the residue washed with acetone. Evaporation of the combined filtrate and washings to remove the acetone gave a residue to which water was added. The aqueous solution was extracted with ether (4 × 20 c.c.), and the extract evaporated to yield only a small amount of residue (0·14 g.). The aqueous solution was concentrated at 40° to dryness and the solid residue was extracted with hot ethyl acetate. Evaporation of this extract to dryness yielded a pale yellow syrup (1·059 g.) which was a mixture (A) (Found: C, 39·0; H, 5·5. Calc. for $C_6H_{11}O_4Cl$: C, 39·5; H, 6·0%) of β-methyl-2-chloro-2-deoxy-D-arabinoside and β-methyl-3-chloro-3-deoxy-D-xyloside.

This mixture of chloro-derivatives (0·099 g.) was dissolved in AnalaR acetic acid (49 c.c.), and 0·0751N-lead tetra-acetate solution (in AnalaR acetic acid) (50 c.c.) was added. The solution was made up to 100 c.c. and oxidation was allowed to proceed at room temperature. At intervals aliquots (10 c.c.) were withdrawn and the extent of oxidation was determined in the usual manner. Results obtained were as follows:

Time (hours)	0·5	1·0	2·0	6·0	19·0
Uptake of $Pb(OAc)_4$ (mols.) ...	0·092	0·111	0·129	0·184	0·184

Attempt to prepare iso*Propylidene Derivatives from the Chloro-derivatives.*—The syrupy mixture (0·763 g.) was shaken with acetone (50 c.c.) containing 0·5% of sulphuric acid. After 12 hours the solution was neutralised with potassium carbonate, then filtered, and the filtrate evaporated to dryness at 35—40°. The syrupy residue (0·7 g.) was placed in solution in ethanol–benzene (1 : 1), on an activated alumina column (12 × 1 cm.). Elution with the same solvent mixture gave only a single fraction, as an extremely viscous pale yellow syrup (0·25 g.), b. p. 135—140° (bath-temp.)/0·008 mm., n_D^{18} 1·4950, $[\alpha]_D^{18}$ −24·3° (*c*, 0·74 in chloroform). It was *β-methyl-3-chloro-3-deoxy-D-xyloside* (Found: C, 39·4; H, 6·2. $C_6H_{11}O_4Cl$ requires C, 39·5; H, 6·0%). When this compound (0·065 g.) in solution in methanol (30 c.c.) was shaken at room temperature for either 5 or 7 hours in an atmosphere of hydrogen with Raney nickel and diethylamine (2 c.c.), no reaction occurred.

Hydrolysis of the Crude Mixture of Chloro-derivatives.—The syrupy mixture of chloroglycosides (A) (0·201 g.) was heated at 100° with N-hydrochloric acid (20 c.c.). The reaction was followed polarimetrically and the following values for change in optical rotation were observed:

Time (hours)	1	2	3	9	10	11	12
$[\alpha]_D^{21}$	−17·9°	−1·9°	0°	+27·9°	+27·9°	+29·8°	+29·8°

After 12 hours the solution was neutralised with silver carbonate and filtered through a charcoal pad, and the filtrate evaporated to dryness. The residue was extracted with ethanol, and the extract when concentrated gave a clear syrup (0·131 g., 58·7%) which reduced Fehling's solution. A 1% aqueous solution of this syrup was prepared and one drop was run on filter paper (Whatman No. 1) and eluted with butanol–ammonia–water in an atmosphere of butanol–water. (The solvents were prepared from butanol 40%, ethanol 10%, water 49%, and ammonia 1% by separation of the butanol phase, which was used for elution, and the aqueous phase, which was used to saturate the paper.) The chromatogram was developed in the usual way. The result indicated that the original mixture consisted predominantly of β-methyl-3-chloro-3-deoxy-D-xyloside with very faint indications of the presence of the other isomer expected.

Treatment of β-Methyl-2 : 3-anhydro-D-riboside with Lithium Aluminium Hydride.—β-Methyl-2 : 3-anhydro-D-riboside (0·303 g.) was dissolved in absolute ether (40 c.c.) and lithium aluminium hydride (0·6 g.) in absolute ether (20 c.c.) was added. The mixture was heated under reflux in anhydrous conditions for 3 hours and then a further amount of lithium aluminium hydride (0·6 g.) in absolute ether (20 c.c.) was added. Heating was continued for another hour, and then water (40 c.c.) and 5N-sulphuric acid were added cautiously to the well-stirred mixture, which was subsequently filtered. The ethereal layer was separated, the aqueous phase extracted with ether (3 × 40 c.c.), and the extract added to the ethereal layer. Evaporation of the ethereal solution, after being dried ($MgSO_4$), gave a minute amount of residue which gave a negative test with the Dische diphenylamine reagent. The aqueous solution was neutralised with ammonium carbonate and the copious precipitate filtered off and washed with a small amount of water. The filtrate and washings were combined and evaporated to dryness at 40°. The residue was extracted with hot chloroform (6 × 40 c.c.), and evaporation of the extract gave a syrupy residue (0·218 g., 71%) which gave a positive reaction with the Dische diphenylamine reagent. This residue was heated at 100° for 4 hours with N-hydrochloric acid (10 c.c.), and then the solution was neutralised (Ag_2CO_3) and stirred with charcoal. After filtration the solution was concentrated to dryness and the solid residue extracted with ethanol. Evaporation of the extract gave a clear syrup (B) (0·104

g., 60%) which readily reduced Fehling's solution. A 1% aqueous solution of this syrup was run on a paper chromatogram as described above. 1% Aqueous solutions of 2-deoxy-D-ribose and of 3-deoxy-D-xylose were also placed on the same chromatogram and run as standard materials for comparison. The chromatogram was eluted with butanol–water–ammonia, dried, sprayed with aniline hydrogen phthalate and developed by heating at 80—100° for 5 minutes. The developed chromatogram showed the presence of only 3-deoxy-D-xylose in the product from the ring scission of the anhydro-compound (cf. 3-deoxy-D-xylose, R_F 0·498, 2-deoxy-D-ribose, R_F 0·435). This product (0·1036 g.) was then subjected to a milder hydrolysis by treatment with N-hydrochloric acid at room temperature. The following changes in the optical rotation of the solution were observed:

Time (hours)	0	1	3	4	4·5	5·8	7	8	8·75	21	22·5
$[\alpha]_D^{21}$	−92·7°	−92·7°	−90·7°	−89·8°	−88·9°	−83°	−81°	−79·3°	−77·3°	−75·3°	−73·9°

After 23 hours the solution was neutralised with silver carbonate and sodium carbonate, filtered through a charcoal pad, and concentrated to dryness. The residue was extracted with hot ethanol (2 × 25 c.c.), the extract decolorised, and the clear solution concentrated to dryness leaving a syrupy residue (0·0727 g.). A 1% aqueous solution of this syrup (1 drop) was run on a paper chromatogram which was developed with aniline hydrogen phthalate in the usual manner. It showed one spot only, identical with 3-deoxy-D-xylose.

Attempts to use even milder methods for the hydrolysis of the product (0·035 g.) from the ring scission of the anhydro-compound by treatment with 0·01N-acetic acid (5 c.c.) at 100° for 2 hours, followed by evaporation to dryness at room temperature in a vacuum-desiccator over phosphoric oxide and potassium hydroxide, were unsuccessful. When the product from this treatment was run on a paper chromatogram according to the usual procedure, no spots were discernible.

Oxidation by Lead Tetra-acetate.—The syrupy deoxyglycoside mixture (0·1056 g.) was dissolved in AnalaR acetic acid (49 c.c.), and 0·074N-lead tetra-acetate in acetic acid solution (30 c.c.) was added. The solution was made up to 100 c.c. and oxidation allowed to proceed at room temperature. At suitable intervals aliquots (10 c.c.) were withdrawn and titrated iodometrically:

Time (hours)	1	3	4	6	9	23
$Pb(OAc)_4$ absorbed (mols.)	0·084	0·098	0·112	0·126	0·126	0·14

2 : 4-*Ditoluene*-p-*sulphonyl* β-*Methyl*-3-*deoxy*-D-*xyloside*.—The syrupy deoxyglycoside mixture (0·169 g.) in pyridine solution (0·5 c.c.) readily reacted with toluene-*p*-sulphonyl chloride (0·48 g.). The product was purified by passage down an alumina column (20 × 1·5 cm.) and gave crystalline 2 : 4-*ditoluene*-p-*sulphonyl* β-*methyl*-3-*deoxy*-D-*xyloside*, m. p. 89°, $[\alpha]_D^{21}$ −61° (*c*, 0·39 in chloroform) (Found: C, 52·2; H, 5·3. $C_{26}H_{34}O_8S_2$ requires C, 52·6; H, 5·3%) (cf. m. p. 99° for 3 : 4-ditoluene-*p*-sulphonyl β-methyl-2-deoxy-D-riboside).

3-*Deoxy*-D-*xylitol* 1 : 2 : 4 : 5-*Tetrabenzoate*.—The clear syrup (B) (0·347 g.) in solution in water (300 c.c.) was shaken for 18 hours at 100° in an atmosphere of hydrogen (25 atmospheres' pressure) with Raney nickel. After filtration the solution was evaporated to dryness and afforded a syrup (0·258 g.) ($[\alpha]_D^{18}$ ±0° in methanol). This (0·224 g.) was dissolved in absolute pyridine (1 c.c.), and the solution cooled to 0°. Benzoyl chloride (4·4 mols., 1·025 c.c.) was added and the mixture kept at room temperature for 12 hours. Ice-water (50 c.c.) was then added. The syrup which was precipitated was extracted with chloroform, and the extract was washed successively with dilute hydrochloric acid, sodium hydrogen carbonate solution, and water and then dried ($MgSO_4$). Evaporation of the extract gave a syrup which crystallised on nucleation with 3-deoxy-D-xylitol tetrabenzoate, m. p. 104° alone or on admixture with an authentic sample, $[\alpha]_D^{14}$ ±0° in methanol (cf. Kent *et al.*, *loc. cit.*).

Derivatives of 2-*Deoxy*-D-*ribose*.—Acetylation of 2-deoxy-D-ribose (0·296 g.) in pyridine solution (1·65 c.c.) with freshly distilled acetic anhydride (1·08 c.c.) readily gave the 1 : 3 : 4-*triacetyl* derivative as small colourless needles (from methanol), m. p. 98°, $[\alpha]_D^{23}$ −171·8° (*c*, 0·56 in chloroform) (Found: C, 50·8; H, 6·3. Calc. for $C_{11}H_{14}O_7$: C, 50·8; H, 6·2%). Davoll and Lythgoe (*J.*, 1949, 2529) report this compound as a syrup, b. p. 180° (bath-temp.)/0·1 mm., $[\alpha]_D^{17}$ −52·5° (*c*, 2·5 in chloroform).

Similarly 2-deoxy-D-ribose (0·102 g.) affords a 1 : 3 : 4-*tribenzoyl* derivative as small white nodules (from ethanol), m. p. 127°, $[\alpha]_D^{23}$ −65° (*c*, 1·02 in chloroform) (Found: C, 69·9; H, 5·4. $C_{26}H_{22}O_7$ requires C, 69·9; H, 5·0%).

2-*Deoxy*-D-*ribose* p-*nitrophenylhydrazone*, prepared by the usual procedure, had m. p. 160°, $[\alpha]_D^{14}$ −11·1° (*c*, 0·09 in ethanol) (Found: C, 49·1; H, 5·6. $C_{11}H_{15}O_5N_3$ requires C, 49·1; H, 5·6%).

3 : 4-*Ditoluene*-p-*sulphonyl* β-*Methyl*-2-*deoxy*-D-*ribopyranoside*.—Toluene-*p*-sulphonylation of β-methyl-2-deoxy-D-ribopyranoside (0·045 g.) readily yielded the 3 : 4-*ditoluene*-p-*sulphonate* as silky needles (from aqueous ethanol), m. p. 104—107°, $[\alpha]_D^{20}$ −115·5° (*c*, 6·7 in chloroform) (Found: OMe, 6·0. $C_{20}H_{24}O_8S_2$ requires OMe, 6·7%). When this compound (0·034 g.) was heated at 105—110° for 3 hours with dry sodium iodide (0·028 g.) in anhydrous acetone (8 c.c.), no visible reaction occurred and no sodium toluene-*p*-sulphonate separated.

3 : 5-*Ditoluene*-p-*sulphonyl* αβ-*Methyl*-2-*deoxy*-D-*ribofuranoside*.—Prepared by the normal procedure the *ditoluene*-p-*sulphonate* was obtained in syrupy form, $[\alpha]_D$ −121° (*c*, 0·4 in chloroform) (Found: OMe, 7·0. $C_{20}H_{24}O_8S_2$ requires OMe, 6·7%). When this was heated in dry acetone (8 c.c.) with sodium iodide (1·1 mols., 0·085 g.) at 105—110° for 3 hours, rapid precipitation of sodium toluene-*p*-sulphonate occurred. This was collected by filtration in a sintered glass crucible, washed with dry acetone, dried at 120° for 1 hour, and weighed (0·095 g. = 1 mol.).

3 : 4-iso*Propylidene* β-*Methyl-2-deoxy*-D-*ribopyranoside*.—β-Methyl-2-deoxy-D-ribopyranoside (0·1 g.) yielded the **3 : 4-iso*propylidene*** derivative (30 mg.) as a colourless oil, b. p. 110—115°/12 mm., n_D^{20} 1·4456, $[\alpha]_D^{20}$ −47·8° (*c*, 1·04 in water), which gave a positive iodoform test (Found : OMe, 16·0. $C_9H_{16}O_4$ requires OMe, 16·4%).

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340. *Deoxy-sugars. Part XX. The Value of the Dische Test for the Quantitative Determination of Deoxypentose Nucleic Acids.*

By W. G. OVEREND.

The value of the Dische diphenylamine reaction (*Mikrochemie*, 1930, **8**, 4) for the determination of deoxypentosenucleic acids in cellular material has been investigated. It has been shown that amino-acids and purine and pyrimidine bases affect the intensity of the colour developed. Some unsuccessful attempts to modify the reagent are briefly mentioned.

SEVERAL workers (cf. Sevag, Smollens, and Lackmann, *J. Biol. Chem.*, 1940, **134**, 523; Seibert, *ibid.*, 1940, **133**, 593) have used the Dische diphenylamine reaction (*Mikrochemie*, 1930, **8**, 4) for the quantitative determination of deoxyribonucleic acid in cellular material. Hoagland *et al.* (*J. Expti. Med.*, 1940, **72**, 139) estimated the nucleic acid in elementary bodies of vaccinia by using this reaction and stated that the colour produced was stable and that its intensity was proportional to the amount of nucleic acid in the original solution. Recently Hinshelwood and Caldwell (*J.*, 1950, 1415) used the Dische procedure to measure the deoxyribonucleic acid content of *Bact. lactis aerogenes* grown under a variety of conditions.

The test depends on the conversion of the carbohydrate moiety of the nucleic acid into ω-hydroxylævulaldehyde (Deriaz *et al.*, *J.*, 1949, 1222) which then reacts with diphenylamine. Investigations in this Department (*J.*, 1950, 1027) have shown that the test is not specific for 2-deoxy-D-ribose but that it is given by other 2-deoxypentoses. To extend this investigation it was considered worth while to examine the value of the reaction for the quantitative determination of deoxypentose nucleic acid in cellular tissue and bacteria. It is well known that when suitable concentrations (*e.g.*, 0·02—0·2%) of pure deoxypentose nucleic acid are used the intensity of the blue colour developed in the test appears to be proportional to the amount of nucleic acid present. However, Davidson ("The Biochemistry of the Nucleic Acids,"

Effect of added substances on the intensity of colour developed by deoxyribonucleic acid in the Dische test.

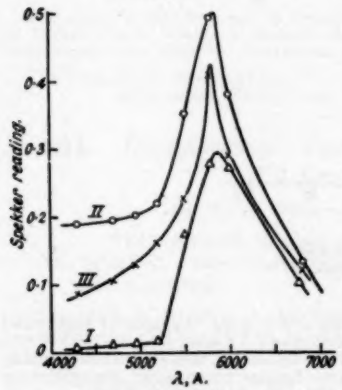
Added substance.	Spekker reading at 5800 A.	Added substance.	Spekker reading at 5800 A.
Amino-acids.			
None	0·280	Tyrosine	0·433
Histidine	0·347	Aspartic acid	0·467
*iso*Leucine	0·363	Arginine	0·470
Serine or lysine	0·373	Phenylalanine	0·480
Alanine	0·400	Leucine	0·510
Cysteine or glycine	0·410	Glutamic acid	0·540
Methionine	0·430	Valine	0·557

Added substance.	$\lambda_{max.}$, A.	Spekker reading.	Added substance.	$\lambda_{max.}$, A.	Spekker reading.
Simple bases.					
None	5950	0·29	Benzylamine	5950	0·51
p-Toluidine	5940	0·47	*iso*Propylamine	5940	0·45
p-Phenylenediamine	5050	0·10	Diethylamine	5950	0·49
Purines and pyrimidines.					
None	5942	0·30	Uracil	5942	0·335
Adenine	5835	0·44	Thymine	5942	0·355
Guanine	5830	0·39	Cytosine	5942	0·380

Methuen Monographs, 1950, p. 60) states that most of the colorimetric sugar reactions are liable to interference by proteins, and hence it is best to remove the protein residue of the tissue before applying the colorimetric tests. Moreover, Webb (personal communication) has shown that the Dische colour is influenced by various concentrations of sodium chloride, but that the effect is not linear.

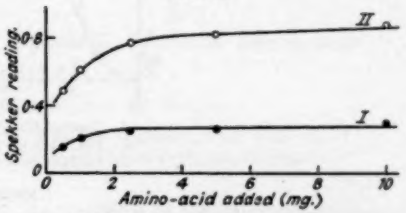
Comparative Dische tests were carried out according to the method described by Deriaz *et al.* (*loc. cit.*), using deoxyribonucleic acid (isolated from soft herring roes by Mirsky and Pollister's method) as control and with other samples of the same nucleic acid to which had been added separately half its weight of protamine and histone. The intensities of the colours developed were measured in the Spekker photoelectric absorptiometer, with Ilford filters 601—608 (λ, 4300—6800 A.). Results are represented in Fig. 1 and show that both proteins enhance the intensity of the colour produced. Since in the acid medium used proteins would be hydrolysed, a series of amino-acids were next tested, with results shown in the Table. In all cases the colour intensity was enhanced. Simple amines had the same effect, although *p*-phenylenediamine interfered with the colour produced and instead of blue a pink colour resulted. Finally, those purine and pyrimidine bases which would be present whenever the

FIG. 1.



I. *Control. Deoxyribonucleic acid* (DRNA) *alone.*
II. DRNA + *protamine.*
III. DRNA + *histone.*

FIG. 2.



I. DRNA *with glycine added.*
II. DRNA *with* DL-*valine added.*

test is used to estimate nucleic acid contents of cellular material were shown to increase the intensity of colour. The effect of the purines was greater than that of the pyrimidines, but neither group of compounds had as great an effect as the amino-acids. Finally, by using glycine and DL-valine the effect of the concentration of the amino-acids on the intensity was examined (see Fig. 2).

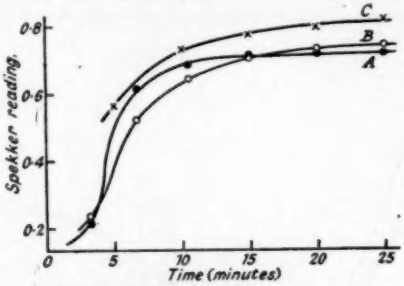
In the procedure adopted by Deriaz *et al.* (*loc. cit.*) the mixture of the nucleic acid and Dische reagent was heated at 100° for 3·25 minutes and we have mainly used this method. However, Woodhouse (*Brit. J. Cancer*, 1949, **3**, 510) concluded that in this period not all the deoxypentose nucleic acid had reacted and stated that 15 minutes' heating was necessary to get a maximum colour. Hinshelwood and Caldwell (*loc. cit.*) and Hoagland *et al.* (*loc. cit.*) found 10 minutes' heating to suffice for maximum colour development. Since our experiments were comparative, under rigidly controlled conditions, the time of heating was immaterial provided that it was sufficiently prolonged to give a colour measurable with accuracy on the Spekker instrument. However, we would state that we agree with Woodhouse, if measurements are to be made of the concentrations of nucleic acid solutions. Fig. 3 illustrates this contention. Moreover it shows also that in experiments with added amino-acid the colour is fully developed in this period.

The results obtained show that great caution must be exercised before using this test for the accurate determination of deoxypentose nucleic acid in cellular material because of the interference of other substances also likely to be present, such as amino-acids, purines, and pyrimidines. The method can, of course, be used to determine the deoxypentose nucleic acid in

pure solutions of unknown concentration. The results reported do not necessarily invalidate earlier work described in which this method of estimation was used. Much of this earlier work was merely comparative and not of great accuracy. Results of Hinshelwood and Caldwell's later work (*loc. cit.*) can only be accurate if errors are constant throughout or cancel each other out. However, their general conclusions are not materially altered since the effects now reported are within the limits of their experimental error.

During this work several unsuccessful attempts were made to prepare modified Dische reagents which would prove more suitable. Replacement in the reagent of the concentrated sulphuric acid by either trichloroacetic or trifluoracetic acid resulted in no colour formation when the test was made in the normal manner. If concentrated hydrochloric acid was used instead of concentrated sulphuric acid the reagent gave a colour when heated with deoxyribonucleic acid, but this was less intense than that obtained with the normal reagent. The addition of phosphate ions to the normal reagent had no effect on the intensity.

FIG. 3.



A. Control (DRNA *alone*).
B. DRNA *with glutamic acid added.*
C. DRNA *with* DL-*valine added.*

EXPERIMENTAL.

Dische Tests.—(a) *Control.* Herring roe deoxypentosenucleic acid (1·6 mg.) (isolated by Mirsky and Pollister's method) was dissolved in water (3 c.c.), and Dische reagent (cf. Deriaz *et al.*, *loc. cit.*) (6 c.c.) was added. The mixture was heated on a boiling water-bath for 3·25 minutes, then cooled for 5 minutes, and the intensity of the blue colour developed was measured in the Spekker photoelectric absorptiometer with Ilford filters 601—608 (λ, 4300—6800 A.). The experiments were conducted in duplicate.

λ, A.	4300	4700	4900	5200	5500	5800	6000	6800
Average Spekker reading	0·005	0·014	0·019	0·070	0·178	0·280	0·275	0·100

(b) *With added proteins.* The experiments were repeated in precise detail except that in one series of tubes protamine (0·8 mg.; B.D.H.) was added, and to another series histone (0·8 mg.). Results are shown in Fig. 1.

(c) *With added amino-acids.* In another series of experiments amino-acids (0·8 mg.) were added. In other respects the conditions were identical with those described. Experiments, conducted in duplicate, are reported in the Table (p. 1484).

(d) *With amines added.* Tubes were prepared each containing deoxyribonucleic acid (1·6 mg.) in water (3 c.c.) and Dische reagent (6 c.c.). To duplicate sets of tubes simple amines (0·8 g.) were added. Results are in the Table.

(e) *With purines and pyrimidines added.* A similar procedure was adopted using 0·8 mg. of adenine, guanine, uracil, cytosine, and thymine. Results are shown in the Table.

Effect of the Amino-acid Concentration on the Intensity of the Dische Colour.—Tubes were prepared each containing herring roe deoxyribonucleic acid (1·6 mg.) in water (1 c.c.) and Dische reagent (4 c.c.). To duplicate sets of tubes glycine solution (1 c.c.) of varying concentration was added. The tubes were heated in a boiling water-bath for 3·25 minutes, then cooled for 5 minutes, and the intensity of colour measured on the Spekker Photoelectric Absorptiometer using Ilford filter no. 606 (cf. Fig. 2).

Glycine added (mg.)	10·0	5·0	2·5	1·0	0·5
Average Spekker reading	0·312	0·279	0·255	0·223	0·184

The experiment was repeated using DL-valine instead of glycine.

DL-Valine added (mg.)	10·0	5·0	2·5	1·0	0·5	0·2
Average Spekker reading	0·881	0·830	0·784	0·610	0·490	0·433

Rate of Development of Dische Colour.—(a) *Control.* Herring roe deoxyribonucleic acid (8·2 mg.) was dissolved in water (13 c.c.), and Dische reagent (26 c.c.) was added. The solution was heated at 100° and at noted intervals of time aliquots (5 c.c.) were withdrawn and the intensity of colour was

measured on the Spekker photoelectric absorptiometer using Ilford filter no. 606. Results are shown in Fig. 3.

(b) *With glutamic acid added.* A similar procedure was adopted with a solution containing deoxyribonucleic acid as in (a) (8·2 mg.), and glutamic acid (4·0 mg.) in Dische reagent (26 c.c.) and water (13 c.c.). See Fig. 3 for results.

(c) *With* DL-*valine added.* The procedure was repeated on a solution prepared by dissolving deoxyribonucleic acid (6·66 mg.) and DL-valine (9·6 mg.) in water (12 c.c.) and Dische reagent (21·2 c.c.). Results are represented in Fig. 3.

Attempts to Prepare a Modified Dische Reagent.—(*a*) Twice recrystallised diphenylamine (0·4 g.) was added to AnalaR acetic acid (40 c.c.) and trichloroacetic acid (1·1 c.c.). This reagent (4 c.c.) was added to a solution of deoxyribonucleic acid (1·6 mg.) in water (2 c.c.), and the solution was heated at 100° for 3·25 minutes and then cooled. No colour developed. A similar result was obtained if trifluoracetic acid was used instead of trichloroacetic acid.

(*b*) Twice recrystallised diphenylamine (0·4 g.) was added to AnalaR acetic acid (40 c.c.) and concentrated hydrochloric acid (1·1 c.c.). Deoxyribonucleic acid (1·6 mg.) was added to water (3 c.c.) containing this reagent (6 c.c.). After being heated at 100° for exactly 3·25 minutes the solution was cooled and the colour intensity measured in the usual manner.

λ, A.	4300	4700	4900	5200	5500	5800	6000	6800
Spekker reading	0·043	0·052	0·086	0·111	0·132	0·172	0·155	0·075

(Cf. control experiments on p. 1486 using the normal reagent.)

The author thanks Professor M. Stacey, F.R.S., for his continued interest in this work, the Board of the British Rubber Producers' Research Association for financial assistance, and Miss P. M. Hudson for valuable assistance with the experimental work.

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341. *Deoxy-sugars. Part XXI. Synthesis of Some Derivatives of 2-Deoxy-*D*-galacturonic Acid.*

By W. G. OVEREND, F. SHAFIZADEH, and M. STACEY.

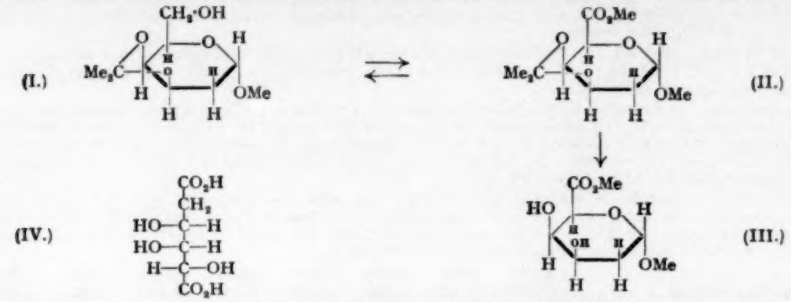
The synthesis of some derivatives of 2-deoxy-D-galacturonic acid is described. Their conversion into the monolactone of 2-deoxygalactosaccharic acid is outlined.

DURING work in progress in this Department on the chemistry of the hexuronic acids and particularly on the mechanism of the Tollens naphtharesorcinol diagnostic reaction for acids of this class (cf. Tollens, *Ber.*, 1908, **41**, 1788; Mayer, Block, and Chaffee, *Fed. Proc.*, 1942, **1**, 125; Hanson, Mills, and Williams, *Biochem. J.*, 1944, **38**, 274; Guerrero and Williams, *Nature*, 1948, **161**, 930; Ogata and Nozaki, *J. Pharm. Soc. Japan*, 1943, **63**, 416; 1944, **64**, 14) it became necessary to prepare hexuronic acid derivatives suitably protected at $C_{(2)}$ so that this site in the molecule would not undergo reaction. Derivatives of the hitherto unknown 2-deoxyhexuronic acids seemed suitable for this purpose. Further it is well known that hexuronic acids can undergo intramolecular changes under alkaline conditions (Smith, *J.*, 1944, 510, 577) and it was considered likely that the 2-deoxyhexuronic acid derivatives might be of particular interest in investigating these changes.

Ohle and Berend (*Ber.*, 1925, **58**, 2585) described a method whereby uronic acid derivatives could be easily prepared. They converted 1 : 2-3 : 4-di*iso*propylidene D-galactose into 1 : 2-3 : 4-di*iso*propylidene D-galacturonic acid by oxidation with alkaline potassium permanganate. Similarly Ault, Haworth, and Hirst (*J.*, 1935, 517) used the method to convert 2 : 3-*iso*propylidene α-methylmannoside into 2 : 3-*iso*propylidene α-methylmannuronoside (cf. Stacey, *J.*, 1939, 1529). Recently the preparation of 3 : 4-*iso*propylidene α-methyl-2-deoxy-D-galactoside (I) was described (*J.*, in the press) and it was expected that this would be a suitable starting material for the preparation of derivatives of 2-deoxygalacturonic acid.

3 : 4-*iso*Propylidene α-methyl-2-deoxy-D-galactoside (I) was prepared from α-methyl-2-deoxy-D-galactoside by treatment with acetone and zinc chloride. It was characterised as its 6-*p*-nitrobenzoate. The galactoside (I) was oxidised under appropriate conditions with a solution of potassium permanganate and aqueous potassium hydroxide, affording 3 : 4-*iso*propylidene α-methyl-2-deoxy-D-galacturonoside as its potassium salt. This was immediately treated with diazomethane in ethereal solution and gave the crystalline methyl ester (II), which could be prepared alternatively by treating the potassium salt with an excess of methyl iodide. It gave a strong naphtharesorcinol test. When (II) was kept in 1% methanolic hydrogen chloride, scission of the *iso*propylidene residue occurred and α-methyl-2-deoxy-D-galacturonoside

methyl ester (III) was obtained in crystalline form. It was readily converted into the corresponding amide by methanolic ammonia. Although both (II) and (III) readily gave the



Tollens naphtharesorcinol reaction for hexuronic acids, neither gave the brick-red colour with basic lead acetate which was described by Stacey (*loc. cit.*) as specific for galacturonic acid.

When 2-deoxy-D-galactose was oxidised with nitrogen tetroxide it yielded a crystalline derivative which elemental analysis indicated was a monolactone of 2-deoxy-D-galactosaccharic acid (IV). This was also prepared by oxidation with bromine of relatively crude 2-deoxy-D-galacturonic acid, itself prepared by acidic hydrolysis of 3 : 4-*iso*propylidene α-methyl-2-deoxy-D-galacturonoside methyl ester (II). The monolactone gave a crystalline acridine salt. It is interesting that 2-deoxy-D-galactosaccharic acid gives a monolactone, since the corresponding galactosaccharic acid cannot readily be made to undergo lactone formation. The monolactone, after treatment with dilute aqueous alkali, did not reduce hot Fehling's solution, thereby indicating that isomerisation to an unsaturated compound such as occurs with glucosaccharo-1 : 5-3 : 6-dilactone and mannosaccharodilactone (Smith *et al.*, *loc. cit.*) had not taken place.

The syntheses herein described, coupled with that of 2-deoxy-D-galactonic acid (*J.*, 1950, 671), make the main oxidation products of 2-deoxy-D-galactose available for study and use in synthetic operations. Further work on the Tollens reaction will be reported later.

Recently Lythgoe and Trippett (*J.*, 1950, 1983) elaborated a method for the identification of methylated uronic acid derivatives in which they are converted into methylated aldoses by making use of lithium aluminium hydride to effect the reduction $CO_2Me \longrightarrow CH_2{\cdot}OH$. This method was extended by Smith *et al.* (*Nature*, 1950, **166**, 1037). We had independently applied it in the present work and have been able to demonstrate that lithium aluminium hydride in ethereal solution reduces (II) to 3 : 4-*iso*propylidene α-methyl-2-deoxy-D-galactoside (I).

Experimental.

3 : 4-iso*Propylidene* α-*Methyl*-2-*deoxy*-D-*galactopyranoside*.—α-Methyl-2-deoxy-D-galactoside (2·4 g.) was mechanically shaken for 3 days with dry acetone (50 c.c.) and zinc chloride (8 g.). The product was isolated in the manner described earlier (Overend, Foster, and Stacey, *J.*, 1951, 974). The *iso*propylidene derivative was obtained as a colourless syrup (1·5 g.), b. p. 105—110° (bath-temp.)/0·008 mm., n_D^{19} 1·4689, $[\alpha]_D^{18}$ +94·6° (*c*, 0·76 in ethanol).

This derivative (0·404 g.) and *p*-nitrobenzoyl chloride (0·315 g.) were dissolved in dry pyridine (5 ml.). After 5 hours at room temperature the solution was poured into water. The solid which separated was collected and recrystallised from aqueous methanol. The 6-p-*nitrobenzoate* had m. p. 96°, $[\alpha]_D^{18}$ +56·3° (*c*, 1·03 in methanol) (Found: C, 55·8; H, 5·5. $C_{17}H_{21}O_9N$ requires C, 55·5; H, 5·7%).

3 : 4-iso*Propylidene* α-*Methyl*-2-*deoxy*-D-*galacturonoside Methyl Ester*.—(*a*) 3 : 4-*iso*Propylidene α-methyl-2-deoxy-D-galactoside (1·4 g.) was treated with a solution of potassium permanganate (2·8 g.) in aqueous potassium hydroxide (0·75 g. in 100 c.c. of water). The solution immediately became green, and then brown (manganese dioxide). After 20 hours at room temperature the mixture was filtered, and the filtrate neutralised with carbon dioxide and then evaporated to dryness under diminished pressure. After a preliminary extraction with ether (30 c.c.) the residue was extracted with dry ethanol. The ethanolic extract was evaporated to dryness and afforded a syrupy residue, which gave a strong Tollens naphtharesorcinol test for uronic acids. This syrup was dissolved in dry acetone (20 c.c.) and precipitated by addition of an equal volume of dry ether, as a hygroscopic amorphous powder (1·67 g.). After dissolution in water (10 c.c.) this powder was treated with 0·5N-sulphuric acid (6·24 c.c.). The acidic solution was immediately extracted with ether (5 × 60 c.c.). The extract was washed with water, dried ($MgSO_4$), and concentrated. The residue was then treated with an excess of diazomethane in ether (200 c.c.). After 2 days in a dry atmosphere the solution was filtered and the filtrate evaporated at room temperature. The solid residue was recrystallised from dry ether and 3 : 4-iso*propylidene* α-*methyl*-2-*deoxy*-D-*galacturonoside methyl ester* (0·42 g.) was obtained as colourless needles, m. p. 132—133·5°, $[\alpha]_D^{18}$ +16·8° (*c*, 0·77 in methanol) (Found: C, 53·8; H, 7·5. OMe, 25·9. $C_{11}H_{18}O_6$ requires C, 53·7; H, 7·3; OMe, 25·2%). This ester gave a strong naphtharesorcinol test.

(*b*) 3 : 4-*iso*Propylidene α-methyl-2-deoxy-D-galactoside (8·8 g.) was added to a solution of potassium permanganate (15 g.) and potassium hydroxide (9·5 g.) in water (400 c.c.). Next morning the mixture was filtered and the filtrate evaporated to dryness. The residue was washed with ether to remove unchanged material and potassium 3 : 4-*iso*propylidene α-methyl-2-deoxy-D-galacturonate was obtained by extraction with dry methanol and evaporation of the extract. It was dissolved in dry methanol (50 c.c.) and the solution heated under reflux for 3 hours with excess of methyl iodide (15 c.c.). The solvent and remaining methyl iodide were removed by evaporation and the residue was extracted by boiling under reflux with ether (4 × 50 c.c.). The residue after this extraction was re-treated with methanol and methyl iodide and the above procedure followed. This procedure was repeated twice more. The combined ethereal extracts were evaporated to dryness and the solid residue was recrystallised from dry ether; 3 : 4-*iso*propylidene α-methyl-2-deoxy-D-galacturonoside methyl ester (3·9 g.) was obtained as colourless needles, m. p. 132—133·5° alone or on admixture with the above sample.

α-*Methyl-2-deoxy-*D-*galacturonoside Methyl Ester.*—3 : 4-*iso*Propylidene α-methyl-2-deoxy-D-galacturonoside methyl ester (2·5 g.) was dissolved in 1% methanolic hydrogen chloride (25 c.c.) and set aside for 7 hours. Then the solution was neutralised with silver carbonate and filtered through a charcoal pad. The filtrate was evaporated to dryness and the syrupy residue crystallised on trituration with ethyl acetate. Repeated recrystallisation from ethyl acetate afforded α-*methyl-2-deoxy-*D-*galacturonoside methyl ester* (1·2 g.) as colourless needles, m. p. 111°, $[\alpha]_D^{17}$ +128° (*c*, 1·25 in methanol) (Found : C, 46·3; H 6·8. $C_8H_{14}O_6$ requires C, 46·6; H, 6·8%).

α-*Methyl-2-deoxy-*D-*galacturonoside Amide.*—α-Methyl-2-deoxy-D-galacturonoside methyl ester (0·128 g.) was dissolved in absolute methanol saturated with dry ammonia and the solution set aside for 17 hours at room temperature. Evaporation of the solvent gave a solid residue which on recrystallisation from ethyl acetate afforded the *amide* (0·086 g.) as colourless needles, m. p. 203°, $[\alpha]_D^{16}$ +105·4° (*c*, 1·1 in methanol) (Found : C, 44·02; H, 6·7. $C_7H_{13}O_5N$ requires C, 43·97; H, 6·8%).

Monolactone of 2-*Deoxy-*D-*galactosaccharic Acid.*—(*a*) 2-Deoxy-D-galactose (1·5 g.) was treated with dry nitrogen tetroxide (3 c.c.) at 0° in a dry atmosphere. After 18 hours the nitrous gases were removed by evaporation under diminished pressure initially at room temperature and then at 50°. The residual syrup was dissolved in ethyl acetate, and the solution was re-evaporated. This procedure was repeated several times to ensure complete removal of nitrous gases. The syrup finally obtained, which was non-reducing towards hot Fehling's solution, was dissolved in water (15 c.c.) and treated with excess of silver oxide. Filtration and evaporation of the filtrate afforded material which was washed with absolute ethanol to remove syrupy products. The dry material was then dissolved in water (20 c.c.) and the solution filtered through a charcoal pad. Thereafter hydrogen sulphide was passed through the filtrate and the precipitate separated. After re-evaporation the dry residue was extracted with acetone. Removal of the solvent afforded a syrup which crystallised on trituration with ether. Recrystallisation from acetone–ether afforded the *monolactone* (150 mg.), m. p. 155—157° (indefinite), $[\alpha]_D^{21}$ −43·4° (constant for 6 days) (*c*, 1·15 in water) (Found : C, 40·8; H, 4·6. $C_6H_8O_6$ requires C, 40·9; H, 4·5%).

(*b*) 3 : 4-*iso*Propylidene α-methyl-2-deoxy-D-galacturonoside methyl ester (0·5 g.) in 0·01% hydrochloric acid (20 c.c.) was heated at 100° for an hour (after this time the optical rotation was constant). Silver carbonate was added to effect neutralisation. After filtration the filtrate was treated with hydrogen sulphide and refiltered. Evaporation of the filtrate to dryness, followed by extraction of the residue with absolute methanol and concentration of the extract, afforded a syrup (0·24 g.) which could not be induced to crystallise. It was strongly reducing towards Fehling's reagent. The syrup was dissolved in water (5 c.c.) and bromine (0·5 c.c.) was added. After 4 days, excess of bromine was removed by aeration and the solution was neutralised by addition of silver oxide. The precipitate was removed and the filtrate evaporated to dryness. The residue was heated under reflux with methanol (15 c.c.) and then filtered. The precipitate was washed with absolute methanol followed by ether and was then redissolved in water (2 c.c.). Hydrogen sulphide was passed through the solution which was then filtered through a charcoal pad. The lactone (0·05 g.), isolated from the filtrate in the manner already described, had m. p. 155—157° alone or on admixture with the sample prepared by the previous method.

The monolactone (59 mg.) and acridine (60 mg.) in dry methanol (1·0 c.c.) were heated at 60° for 5 minutes. Thereafter ether was added. A precipitate formed and was collected. Recrystallisation from methanol–ether afforded the *monoacridine* salt (75 mg.), m. p. 148°, $[\alpha]_D^{19\cdot5}$ −25·3° (*c*, 2·1 in methanol) (Found : C, 63·9; H, 4·9. $C_6H_8O_6.C_{13}H_9N$ requires C, 64·2; H, 4·8%).

Reduction of 3 : 4-iso*Propylidene* α-*Methyl-2-deoxy-*D-*galacturonoside Methyl Ester with Lithium Aluminium Hydride.*—3 : 4-*iso*Propylidene α-methyl-2-deoxy-D-galacturonoside methyl ester (1 g.) and finely powdered lithium aluminium hydride (1·2 g.) in dry ether (200 c.c.) were heated under reflux for 5 hours. After the solution had been cooled, water (10 c.c.) was added, followed by excess of 5N-hydrochloric acid (15 c.c.). The mixture was vigorously agitated and then immediately neutralised by the addition of sodium hydrogen carbonate. The ethereal layer was separated and the aqueous residue further extracted with ether (3 × 150 c.c.). The combined extracts were dried ($MgSO_4$) and the solvent was evaporated under diminished pressure. The syrupy residue was distilled as a colourless syrup (0·2 g.), b. p. 105—110° (bath-temp.)/0·05 mm., n^{15} 1·4685 (Found : C, 54·4; H, 8·1; OMe, 15·0. Calc. for $C_{10}H_{18}O_5$: C, 55·0; H, 8·3; OMe, 14·3%). It was 3 : 4-*iso*propylidene α-methyl-2-deoxy-D-galactopyranoside.

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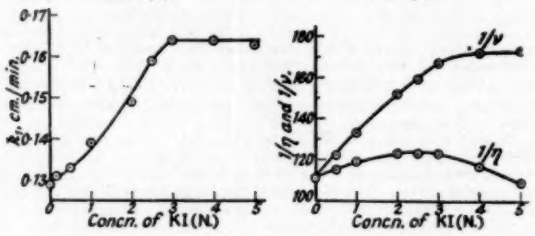
342. *The Kinetics of the Dissolution of Zinc in Aqueous Iodine Solutions. Part II.*

By L. L. Bircumshaw and A. C. Riddiford.

An increase in the concentration of potassium iodide produces a marked increase in the rate of dissolution of zinc in aqueous iodine solutions. This increase is comparable with the increase in the coefficient of diffusion of iodine under the same conditions, and both have been correlated with the decrease in the kinematic viscosity, ν, of the solution. By varying the viscosity of the solutions it is shown that the relation between the observed rate constant per unit area per unit volume, k_1, and ν at 25° may be expressed: k_1 (cm. min.$^{-1}$) $= 0{\cdot}00342(1/\nu)^{0{\cdot}75}$. The observed rate is at least partly determined by the rate of transport of iodine to the zinc surface; it is independent of the rate of recession of products from the surface.

The results reported in Part I (*J.*, 1951, 598) are consistent with the view that the observed rate of dissolution of zinc in aqueous iodine solutions is at least partly determined by the rate of a transport process. The observed rate should therefore be a function of the viscosity of the solution. Van Name and Hill (*Amer. J. Sci.*, 1913, **36**, 543) have shown this to be the case for the dissolution of cadmium in such solutions, but were unable to establish the relation between the observed velocity constant and the viscosity.

Fig. 1(*a*). Fig. 1(*b*).



In view of the importance of the point, and the fact that Edgar and Diggs (*J. Amer. Chem. Soc.*, 1916, **38**, 253) and Miller (*Proc. Roy. Soc.*, 1924, *A*, **106**, 724) experienced difficulty in correlating the change in the diffusion coefficient of iodine in aqueous iodide solutions with the viscosity, it seemed desirable to study the viscous effect in some detail. Accordingly, this part of the present work reports the investigation of the following points: (1) the effect of varying the concentration of potassium iodide; (2) the effect varying the viscosity of the solution by the addition of sucrose; (3) the effect of replacing potassium iodide by other iodides.

Experimental.

The apparatus and experimental method have been described (Part I, *loc. cit.*). The solutions were initially N/25 with respect to iodine and N/100 with respect to sulphuric acid. Zinc specimens (3·0 × 4·0 cm.), polished in the standard manner, were rotated in the solutions at 100 r.p.m. The temperature was 25° ± 0·01°.

Concentration of Potassium Iodide.—The concentration of potassium iodide was varied over the range 0·5—5·0N., the experimental conditions being otherwise standard. An Ostwald viscometer was used to determine the viscosity of the solutions. A correction for the deviation from Poiseuille's law was applied, using the method proposed by Barr ("A Monograph of Viscometry," 1931), whereby the viscometer is calibrated by using a series of liquids of known viscosity.

The observed values of the rate constant per unit area per unit volume, k_1, together with the values of the coefficient of dynamic viscosity, η, kinematic viscosity, and density of the solutions are recorded in Table I. Values of k_1 for runs in which the concentration of potassium iodide was zero and N/6·25, respectively (Table III, Part I), have been included for comparison. In Fig. 1(*a*) the mean values of k_1 are plotted against concentration of potassium iodide. In Fig. 1(*b*) values of the fluidity ($1/\eta$), and of the function $1/\nu$, are similarly plotted.

TABLE I.

KI, g.-equiv./l.	k_1 (obs.), cm. min.$^{-1}$.	Mean k_1, cm. min.$^{-1}$.	d, g./ml.	η, cp.	ν, cs.
0	0·129, 0·129	0·129	0·9972	0·901	0·903
0·16	0·131	0·131	1·0205	0·889	0·870
0·5	0·134, 0·132	0·133	1·0611	0·869	0·819
1·0	0·138, 0·139, 0·139	0·139	1·1176	0·839	0·751
2·0	0·147, 0·149, 0·151	0·149	1·2378	0·816	0·659
2·5	0·158, 0·159	0·159	1·2957	0·814	0·628
3·0	0·163, 0·164	0·164	1·3549	0·813	0·600
4·0	0·164	0·164	1·4699	0·854	0·581
5·0	0·160, 0·166	0·163	1·5852	0·915	0·577

Viscosity of the Solution.—The viscosity of the solutions was increased by the addition of sucrose. Preliminary tests on N/25-iodine which was 1·0M. with respect to sucrose showed that the concentration of iodine remained unchanged at 25° for 3 days. This solution was then made 0·01N. in sulphuric acid, whereafter the iodine titre remained constant for 5 hours.

The results are recorded in Table II. Values of the function $(\Sigma v\Delta \log c)/A$ (see Part I) for one run at each different concentration of sucrose are plotted against time in Fig. 2.

TABLE II.

Sucrose, g.-mol./l.	k_1 (obs.), cm. min.$^{-1}$.	Mean k_1, cm. min.$^{-1}$.	d, g./ml.	η, cp.	ν, cs.
0	0·131	0·131	1·0205	0·889	0·870
0·25	0·108, 0·105	0·107	1·0551	1·124	1·065
0·5	0·0857, 0·0854	0·0856	1·0832	1·462	1·350
0·75	0·0684, 0·0690	0·0687	1·1182	1·992	1·782
1·0	0·0524, 0·0530	0·0527	1·1441	2·836	2·479
1·5	0·0291, 0·0289	0·0290	1·2039	6·610	5·490
2·0	0·0140, 0·0144	0·0142	1·2447	20·64	16·58

Other Iodides.—The effect of replacing potassium iodide by other iodides was investigated. May and Baker "Laboratory" grade sodium and ammonium iodides were used without further purification. Zinc iodide solutions were prepared from "AnalaR" zinc and hydriodic acid. The effect of each iodide was studied at three concentrations. In addition, k_1 was determined for a solution which was 4N/25 with respect to potassium iodide and 4M/25 with respect to zinc iodide. The results are recorded in Table III.

TABLE III.

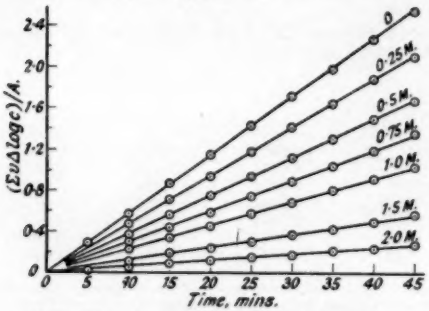
Iodide, g.-equiv./l.	k_1 (obs.), cm. min.$^{-1}$.	Mean k_1, cm. min.$^{-1}$.	d, g./ml.	η, cp.	ν, cs.
		Sodium iodide.			
0·16	0·129, 0·131	0·130	1·0210	0·908	0·889
1·0	0·130, 0·131	0·131	1·1141	0·928	0·833
2·0	0·138, 0·139	0·139	1·2296	0·967	0·786
		Ammonium iodide.			
0·16	0·132, 0·129	0·131	1·0167	0·891	0·876
1·0	0·139	0·139	1·0919	0·840	0·769
2·0	0·152, 0·153	0·153	1·1823	0·900	0·677
		Zinc iodide.			
0·32	0·127, 0·127	0·127	1·0396	0·940	0·904
0·5	0·123, 0·125	0·124	1·0698	0·968	0·905
1·0	0·121, 0·121	0·121	1·1362	1·042	0·917
		Zinc iodide (+ 4N/25-KI).			
0·32	0·126, 0·127	0·127	1·0648	0·934	0·877

DISCUSSION.

An increase in the concentration of potassium iodide results in an increase in the observed rate. Similar results have been reported by Van Name and Edgar (*Amer. J. Sci.*, 1910, **29**, 237) and by Bircumshaw and Everdell (*J.*, 1942, 568). These authors have noted the similarity between the increase in the velocity constant and in the coefficient of diffusion of iodine, D, under the same conditions. Edgar and Diggs's values for D at 25° (*loc. cit.*) are plotted in Fig. 3, which may be compared with Fig. 1(*a*). Miller (*loc. cit.*) found a similar increase in D at 19·91°. Edgar and Diggs, and Miller, found difficulty in correlating this increase in D with variation in the viscosity of the solution. Miller, in particular, stated that the Stokes–Einstein relation is not applicable to this system.

Now potassium iodide belongs to the class of electrolytes exhibiting the characteristic of so-called negative viscosity (see Rabinovich, *J. Amer. Chem. Soc.*, 1922, **44**, 954; Hatschek, "The Viscosity of Liquids," 1928, p. 125). Examination of the results reported in Table I shows that as the concentration of potassium iodide is increased the viscosity of the solution passes through a minimum at *ca.* 2·5N. At high concentrations the solutions are more viscous than water. Thus the plot of the fluidity of the solution against iodide concentration [Fig. 1(*b*)] bears no resemblance to the corresponding plots of D and k_1. On the other hand, the plot of the function $1/\nu$, which may be termed the kinematic fluidity, against concentration is distinctly similar in shape to the plots of D and k_1, a limiting value being reached in each case at *ca.* 3N. For sodium iodide solutions (Table III), the rate increases with increasing salt concentration over the range studied. Over the same range ν decreases whereas η increases.

FIG. 2.



(*Molarities on curves refer to added sucrose.*)

FIG. 3.

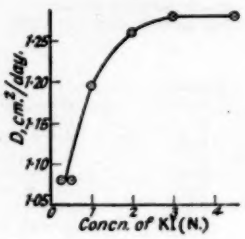


FIG. 4.

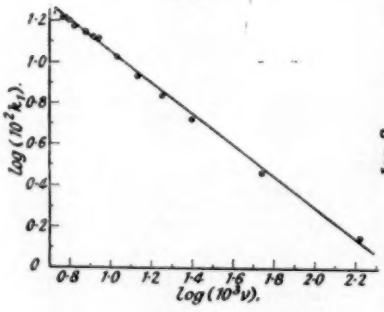
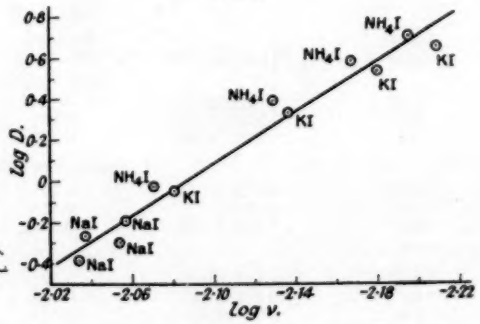


FIG. 5.



Thus it is difficult to escape the conclusion that, for this system at least, the effects are governed by the value of ν rather than of η.

Although the variation in ν is comparatively small, the results are sufficiently accurate to show that neither k_1 nor D is directly proportional to the kinematic fluidity. The results are rather to be expressed by relations of the form $k_1 = \text{constant}(1/\nu)^{\text{const.}}$, where the power is smaller than unity and, on general grounds, is assumed to be temperature invariant. Since the temperature coefficients of k_1 and D differ from that of $(1/\nu)$ (Part I, *loc. cit.*), the constant of proportionality will be temperature dependent.

The 15 values of k_1 recorded in Tables I and II correspond to a range in ν from 0·58 to 16·58 centistokes. Application of the method of least squares gives the expression $k_1 = 0{\cdot}00342(1/\nu)^{0{\cdot}78}$. The plot of log k_1 against log ν is shown in Fig. 4; the solid line corresponds to the above expression, and is seen to correlate the results satisfactorily. Moreover the relation expresses the results recorded in Table III with a maximum deviation of 5·4%, the average

deviation being 2·7%. Hence it seems permissible to conclude that the equation expresses the relation between k_1 and ν within the limits of experimental error.

It is of interest to see whether the data for the diffusion of iodine in aqueous solutions may similarly be correlated with ν. Miller's data for the diffusion of iodine in solution of potassium, sodium, and ammonium iodides at 19·91° are the more extensive, and may be expressed as $D_{19\cdot91}$ (cm.²/day) = $0\cdot0486(1/\nu)^{0\cdot63}$. The data plotted logarithmically in Fig. 5 are seen to be expressed reasonably well by the above relation. On the assumption that the power on the viscous term is temperature invariant, Edgar and Diggs's results are reasonably expressed as $D_{25} = 0\cdot0529(1/\nu)^{0\cdot63}$.

It is concluded that the results reported in this paper support the view that the overall rate of reaction between zinc and aqueous solutions of iodine is at least partly determined by the rate of a transport process. Of the two taking place, it is certain that it is the rate of transport of iodine to the surface of the specimen which affects the observed rate, and not the transport of products from the surface. This is shown by the fact that the observed velocity is strictly of the first order with respect to the concentration of iodine in the bulk of the solution over the time interval studied. Moreover the observed lowering of the rate in the presence of added zinc iodide is quantitatively accounted for by the increase in the kinematic viscosity of the solution. Apart from the viscous effect, then, the concentration of product is without effect on the observed rate under the conditions studied.

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343. 2 : 2 : 4- *and* 2 : 4 : 4-*Trimethylcyclopentanone and Some Related Compounds.*

By S. F. Birch and E. A. Johnson.

During the synthesis of 1 : 1 : 3-trimethyl*cyclo*pentane, pure specimens of 2 : 2 : 4- and 2 : 4 : 4-trimethyl*cyclo*pentanone and of their parent acids, αα*γ*- and α*γγ*-trimethyladipic acids, have been isolated and characterised unambiguously. Published information about these compounds is often unsatisfactory. 2 : 2 : 4- and 2 : 4 : 4-Trimethyl*cyclo*pentanol, 1 : 4 : 4- and 3 : 3 : 5-trimethyl*cyclo*pentene, and two 1 : 2 : 4-trimethyl*cyclo*pentanes are also described.

In connection with an investigation into the composition of Iranian naphthas, pure samples of the isomeric trimethyl*cyclo*pentanes were required. The general method adopted for the preparation of substituted *cyclo*pentanes is by cyclisation of the corresponding adipic acid followed by conversion of the resultant ketone into the hydrocarbon through the carbinol and olefin. As starting point for the 1 : 1 : 3-isomer, *iso*phorone was selected since this is now commercially available and can be readily converted into the corresponding 3 : 3 : 5-trimethyl*cyclo*hexanol by catalytic reduction. This *cyclo*hexanol on oxidation with nitric acid yields a mixture of acids in which the major products are αα*γ*- and α*γγ*-trimethyladipic acids. The acids of lower molecular weight formed simultaneously illustrate well the strong resistance to oxidation shown by the *gem*-dimethyl group. From the trimethyladipic acid fraction two acids were obtained which melted at 100° and 69° respectively. Since the higher-melting of these showed a strong tendency to form a monoester and monoanilide under conditions in which the other acid readily yielded a diester and dianilide, it was thought probable that this acid possessed the αα*γ*-structure.

Qudrat-i-Khuda and Ghosh (*J. Indian Chem. Soc.*, 1939, **16**, 287) describe αα*γ*-trimethyladipic acid prepared by two distinct synthetic methods, and give its melting point as 80°. We therefore repeated one of these syntheses and obtained an acid melting at 98°. This value was not raised by recrystallisation but derivatives were obtained which were identical with those from the higher-melting acid from the oxidation products. This identified the acid as αα*γ*-trimethyladipic acid. α*γγ*-Trimethyladipic acid was also synthesised by a method which in its

earlier stages followed work by Qudrat-i-Khuda (*J.*, 1929, 201), and melted at 69°. It was indistinguishable from the corresponding acid from *iso*phorone both in itself and in its derivatives.

Dry distillation of these acids with barium hydroxide gave good yields of the corresponding *cyclo*pentanones. 2 : 2 : 4-Trimethyl*cyclo*pentanone had been described by Wallach (*Annalen*, 1915, **408**, 207; 1924, **437**, 193) from preparations giving no proof of structure, by Qudrat-i-Khuda and Ghosh (*loc. cit.*), and by Sargent (*J. Org. Chem.*, 1942, **7**, 154), and adequately characterised by Sargent. 2 : 4 : 4-Trimethyl*cyclo*pentanone had also been described by Wallach (*Annalen*, 1918, **414**, 332), Dey and Linstead (*J.*, 1935, 1063), and Voitila (*Ann. Acad. Sci. Fennicae*, 1938, **49**, *A*, No. 1, p. 110), but was prepared in each case by methods involving molecular rearrangements.

The trimethyl*cyclo*pentanols obtained from the corresponding ketones by catalytic reduction were dehydrated by activated alumina at 300—325°. Fractional distillation through 40-plate columns showed that the products were mixtures of olefins. Of these one was found to be common to both products and was therefore presumed to be 3 : 3 : 5-trimethyl*cyclo*pentene. This structure was confirmed by oxidation to αα*γ*-trimethylglutaric acid with permanganate.

The product from 2 : 4 : 4-trimethyl*cyclo*pentanol consisted of 3 : 3 : 5-trimethyl*cyclo*pentene mixed with a second olefin. Both yielded 1 : 1 : 3-trimethyl*cyclo*pentane on catalytic hydrogenation; the second should therefore have been 1 : 4 : 4-trimethyl*cyclo*pentene.

From 2 : 2 : 4-trimethyl*cyclo*pentanol a mixture of three olefins was obtained, of which more than half was 3 : 3 : 5-trimethyl*cyclo*pentene. The remaining two olefins on hydrogenation gave stereoisomeric forms of 1 : 2 : 4-trimethyl*cyclo*pentane and were therefore isomeric forms of 1 : 2 : 4-trimethyl*cyclo*pentene.

After the work described above had been completed (1944) further papers appeared describing 2 : 4 : 4-trimethyl*cyclo*pentanone (Naves, *Helv. Chim. Acta*, 1944, **27**, 51; Qudrat-i-Khuda and Mukherji, *J. Indian Chem. Soc.*, 1946, **23**, 435; Chakravarti, *J.*, 1947, 1028). Values quoted for the melting point of the semicarbazone of this ketone still varied from 159° to 168° and, since other discrepancies appeared between our work and that of some of these authors, it was decided to repeat the synthesis of 2 : 4 : 4-trimethyl*cyclo*pentanone described by Chakravarti (*loc. cit.*). The properties of the product obtained agreed quite well with those of our previous preparation. It was observed that the semicarbazones of all the samples examined tended to decompose below the melting points which consequently were dependent on the rate of heating. If this was sufficiently rapid, the value could be as high as 167—168° but was, under normal conditions, in the region of 161—165°. The 2 : 4-dinitrophenylhydrazone was found to be a more reliable derivative for characterisation.

Qudrat-i-Khuda and Mukherji (*loc.c it.*) also described αγγ-trimethyladipic acid giving a melting point of 71°.

Experimental.

Analyses are by Drs. Weiler and Strauss, Oxford. All m. p.s and b. p.s are corrected.

3 : 3 : 5-*Trimethyl*cyclo*hexanol*.—Technical *iso*phorone was hydrogenated in a high-pressure autoclave at 150°, with Raney nickel as catalyst. The yield after distillation under reduced pressure was almost theoretical.

Oxidation of 3 : 3 : 5-*Trimethyl*cyclo*hexanol*.—3 : 3 : 5-Trimethyl*cyclo*hexanol was oxidised by the method given in *Org. Synth.*, Coll. Vol. I., 2nd edn., p. 19, note 5. The molten alcohol was run from a heated funnel into the nitric acid. After removal of nitric acid and water the entire yield of acids was converted into ethyl esters by refluxing it with ethanol in the presence of sulphosalicylic acid. These were then fractionally distilled at 10 mm. through a 25-plate column. Sharply defined fractions were obtained which were identified as shown in the table.

Fraction.	Wt. (%) of crude ester.	B. p./10 mm.	n_D^{20}.	Compound.
1	1·3	80°	1·4175	Ethyl dimethylmalonate.
2	3·7	98	1·4212	Ethyl αα-dimethylsuccinate.
3	9·0	111	1·4275	Ethyl αα*γ*-trimethylglutarate.
4	70	127—128	1·4326	Ethyl trimethyladipates.
Residue	16	>128	—	Monoethyl trimethyladipates.

The mixed esters were hydrolysed with alcoholic potash and the mixed acids recovered in the usual way.

Separation of αα*γ- and* αγγ-*trimethyladipic acids*. The two trimethyladipic acids were separated by fractional crystallisation. They showed a strong tendency to form two liquid phases in aqueous solutions, which was largely avoided by the use of dilute formic acid as a solvent. Although the higher-melting αα*γ*-trimethyladipic acid was less soluble and crystallised out more readily than its isomer, complete separation was not easily effected. For characterisation the acids were recrystallised to constant m. p. from di*iso*propyl ether, or from chloroform–*iso*pentane.

αay-Trimethyladipic acid melts at 100·1—100·5° (Found : C, 57·4; H, 8·4%; equiv., 94·1. Calc. for $C_9H_{16}O_4$: C, 57·4; H, 8·6%; equiv., 94·0). Qudrat-i-Khuda and Ghosh (*loc. cit.*) and Qudrat-i-Khuda and Mukherji (*loc. cit.*) give m. p. 79—80°. The acid (1 g.), heated in aniline (2 g.) for 2 hours, yields mainly a *monoanilide*, m. p. 160·6—161·0° (Found : C, 68·3; H, 7·9; N, 5·2. $C_{15}H_{21}O_3N$ requires C, 68·4; H, 8·0; N, 5·3%), with a little *dianilide* m. p. 169·4—169·8° (Found : C, 74·2; H, 7·6; N, 8·4. $C_{21}H_{26}O_2N_2$ requires C, 74·5; H, 7·7; N, 8·3%). Its diethyl ester has b. p. 123°/9 mm., n_D^{20} 1·4322, d^{20} 0·9694 (Found : C, 64·0; H, 9·9. Calc. for $C_{13}H_{24}O_4$: C, 63·9; H, 9·9%).

αγγ-Trimethyladipic acid melts at 68·6—69·2° (Found : C, 57·2; H, 8·5%; equiv., 93·8). Qudrat-i-Khuda and Mukherji (*loc. cit.*) give m. p. 71°. It forms a *dianilide*, m. p. 162·8—163·3° (Found : C, 74·5; H, 7·5; N, 8·4%), and a diethyl ester, b. p. 124°/9 mm., n_D^{20} 1·4330, d^{20} 0·9703 (Found : C, 64·0; H, 9·9%).

Synthesis of αay-Trimethyladipic Acid.—The synthetic method used to confirm the structure of the *αay*-trimethyladipic acid was one employed by Qudrat-i-Khuda and Ghosh (*loc. cit.*), involving condensation of ethyl mesitonate with ethyl cyanoacetate, reduction of the product to ethyl α-cyano-*αγγ*-trimethyladipate, and acid hydrolysis of the latter. In all but the final stage our results agreed well enough with those of Qudrat-i-Khuda and Ghosh. During the hydrolysis of the cyano-ester with hydrochloric acid a small quantity of volatile oil separated, which proved to be 2 : 2 : 4-trimethyl*cyclo*pentanone. Some cyclisation of the ester must have occurred at an earlier stage, probably during the reduction with amalgamated aluminium. The acid product from the hydrolysis after two recrystallisations from water had m. p. 98°, which was not raised by a further recrystallisation (Found : C, 57·6; H, 8·5%). A mixture of this with the acid from *iso*phorone (melting at 100°) melted at 99°. Refluxing with aniline gave a mono- and a di-anilide, identical with those from the other sample (m. p. and mixed m. p.).

Synthesis of αγγ-Trimethyladipic Acid.—This acid was prepared by a method which also followed in its earlier stages work by Qudrat-i-Khuda (*loc. cit.*). 3 : 3-Dimethyl-5-hexanolactone (CO_2H = 1) was prepared from γ-acetyl-ββ-dimethylbutyric acid by catalytic reduction; the physical constants of the lactone showed an unusual agreement with the values quoted by Qudrat-i-Khuda. Attempts to condense it with potassium cyanide according to Blaise's method (*Bull. Soc. chim.*, 1905, **33**, 899) were unsuccessful. The keto-acid (180 g.) was therefore converted *via* the cyanohydrin by von Auwers's method (*Annalen*, 1896, **292**, 222) into 3 : 3-dimethyl-5-hexanolactone-5-carboxylic acid. The total acid product from the reaction was esterified with methanol and a little hydrochloric acid, and the ester mixture fractionally distilled. After removal of a low-boiling fraction a viscous ester was obtained of b. p. 100°/1·8 mm., n_D^{20} 1·4547, believed to be the methyl ester of the lactonic acid. Hydrolysis of this ester gave the lactonic acid, which after two recrystallisations from benzene–light petroleum melted at 97·2—97·6° (Found : C, 58·1; H, 7·6. Calc. for $C_9H_{14}O_4$: C, 58·2; H, 7·6%). In the subsequent paper by Qudrat-i-Khuda and Mukherji (*loc. cit.*), the same compound was described as melting at 81°. We have repeated their method of preparation and obtained a product melting at 96·7—97·4° after four recrystallisations from ethyl acetate (Found : C, 58·2; H, 7·6%).

3 : 3-Dimethyl-5-hexanolactone-5-carboxylic acid (3 g.) was reduced by heating it under reflux with syrupy phosphoric acid (11 ml.), hydriodic acid (2 ml.), potassium iodide (0·35 g.), and red phosphorus (1 g.). After 12 hours, water (30 ml.) was added and the whole thoroughly extracted with ether. The extract was washed with sodium pyrosulphite solution to remove iodine, then with water, dried, and evaporated. The residue (2 g.) was recrystallised twice from water; the *αγγ*-trimethyladipic acid obtained melted at 68·5—69·5°, and did not depress the m. p. of the corresponding acid from *iso*phorone (Found : C, 57·5; H, 8·6. Calc. for $C_9H_{16}O_4$: C, 57·4; H, 8·6%). It formed a dianilide which was identical with that derived from *iso*phorone (m. p. and mixed m. p.).

Cyclisation of the Trimethyladipic acids.—The trimethyladipic acids were converted into the corresponding cyclic ketones by the procedure described in *Org. Synth.*, Coll. Vol. I, 2nd edn., p. 192, involving dry distillation with 10% (by wt.) of barium hydroxide. The yield was 90%. Pure specimens of the ketones were obtained by fractional distillation at atmospheric pressure through 40-plate fractionating columns, the estimate of purity being determined from the f. p. curves. It was found that some condensation with elimination of water and formation of high-boiling residue always occurred on distillation.

2 : 2 : 4-*Trimethyl*cyclo*pentanone*.—This ketone had b. p. 155·6°/760 mm., n_D^{20} 1·4294, d^{20} 0·8730, f. p. −40·6° (purity 99·7 mole-%) (Found : C, 76·1; H, 11·3. Calc. for $C_8H_{14}O$: C, 76·1; H, 11·2%). The semicarbazone had a more consistent m. p. (170·4—171·1°) than had its isomer (Found : C, 59·3; H, 9·2; N, 22·6. Calc. for $C_9H_{17}ON_3$: C, 59·0; H, 9·3; N, 22·9%). The 2 : 4-*dinitrophenylhydrazone* melts at 164·0—164·6° (Found : C, 55·2; H, 6·0; N, 18·5. $C_{14}H_{18}O_4N_4$ requires C, 54·9; H, 5·9; N, 18·3%). The *p*-nitrobenzylidene derivative melts at 101·2—101·5°; Sargent (*loc. cit.*) gives 99·3—99·5°. The ketone formed as a by-product in the last stage of the synthesis of *αay*-trimethyladipic acid gave a semicarbazone melting at 169·5—170° (uncorr.) (Found : C, 59·2; H, 9·4; N, 22·4. Calc. for $C_9H_{17}ON_3$: C, 59·0; H, 9·3; N, 22·9%). This did not depress the m. p. of the semicarbazone of 2 : 2 : 4-trimethyl*cyclo*pentanone.

2 : 4 : 4-*Trimethyl*cyclo*pentanone*.—This had b. p. 161·5°/760 mm., n_D^{20} 1·4313, d^{20} 0·8765, f. p. −25·6° (purity 99·6 mole-%) (Found : C, 76·3; H, 11·3%). The semicarbazone had m. p. 160—168° depending on heating rate, the 2 : 4-dinitrophenylhydrazone, m. p. 160·6—160·9° (Found : C, 54·9; H, 5·7; N, 17·4%), in excellent agreement with the value given by Naves (*loc. cit.*), and the *p*-nitrobenzylidene derivative, m. p. 122—123·5° (decomp.).

2 : 4 : 4-Trimethyl*cyclo*pentanone was synthesised by Chakravarti's method (*loc. cit.*) with some variations in detail. Dimedone (5 : 5-dimethyl*cyclo*hexane-1 : 3-dione) was oxidised with sodium hypochlorite to ββ-dimethylglutaric acid. The anhydride of this acid was reduced catalytically (copper chromite) to ββ-dimethylvalero-δ-lactone. This was converted *via* the bromo- and cyano-esters into ββ-dimethyladipic acid which was converted by means of sodium into ethyl 2-keto-4 : 4-dimethyl*cyclo*-

pentanecarboxylate. The latter was methylated either without separation from the reaction mixture or after purification, the resulting ethyl 2-keto-1 : 4 : 4-trimethyl*cyclo*pentanecarboxylate being hydrolysed and decarboxylated by refluxing with acid to yield the required ketone.

The best sample of 2 : 4 : 4-trimethyl*cyclo*pentanone from this synthesis boiled at 160·1—160·4° and had n_D^{20} 1·4318—1·4320 (Found : C, 76·4; H, 11·4%). The 2 : 4-dinitrophenylhydrazone had m. p. 160·1—160·6° (Found : C, 55·0; H, 5·9; N, 18·1%).

A further sample of 2 : 4 : 4-trimethyl*cyclo*pentanone was obtained by the Dieckmann condensation of ethyl αγγ-trimethyladipate (from *iso*phorone) with sodium followed by hydrolysis of the 2-keto-1 : 4 : 4-trimethyl*cyclo*pentanecarboxylate [2 : 4-dinitrophenylhydrazone, m. p. 160·6—160·9° (Found : C, 55·2; H, 5·9; N, 17·8%)].

Mixed m. p.s showed that the three samples of 2 : 4 : 4-trimethyl*cyclo*pentanone gave identical 2 : 4-dinitrophenylhydrazones; the derivative of 2 : 2 : 4-trimethyl*cyclo*pentanone depressed their m. p.s.

*Oxidation of the Trimethyl*cyclo*pentanones.*—The structures of the two ketones were finally checked by oxidation with acid dichromate (140 g. of potassium dichromate per l. of 16% sulphuric acid). By a quantity of oxidising agent equiv. to 2 atoms of oxygen per mole of ketone, 2 : 2 : 4-trimethyl*cyclo*pentanone was oxidised partly to αα*γ*-trimethylglutaric acid (m. p. and mixed m. p.). 2 : 4 : 4-Trimethyl*cyclo*pentanone was oxidised completely to a liquid product which was esterified. The ester gave a semicarbazone, m. p. 112°, and a 2 : 4-dinitrophenylhydrazone, m. p. 55·5°, which did not depress the m. p.s of the corresponding derivatives of ethyl γ-acetyl-ββ-dimethylbutyrate. These results were in complete agreement with the expected structures.

2 : 2 : 4- *and* 2 : 4 : 4-*Trimethyl*cyclo*pentanols.*—These were obtained in almost theoretical yields by catalytic reduction of the ketones in a high-pressure autoclave at 95—140°, with Raney nickel as catalyst. Both products appeared to be mixtures of geometrical isomers, and no attempt was made to separate these. 2 : 2 : 4-*Trimethyl*cyclo*pentanol* boiled at 113—116·3°/149 mm. and had n_D^{20} 1·4461 (Found : C, 74·7; H, 12·7. $C_8H_{16}O$ requires C, 74·9; H, 12·6%). 2 : 4 : 4-*Trimethyl*cyclo*pentanol* boiled at 115—118·5°/152 mm. and had n_D^{20} 1·4439 (Found : C, 74·7; H, 12·8%).

Dehydration of 2 : 2 : 4- *and* 2 : 4 : 4-*Trimethyl*cyclo*pentanols.*—This was accomplished by passing the carbinols over activated alumina (10—14 mesh) at 300—325° at a rate of about 0·2 v./v./hour.

The product obtained from 2 : 2 : 4-trimethyl*cyclo*pentanol contained about 60% of one olefin and 10—15% of each of two higher-boiling olefins. That obtained from 2 : 4 : 4-trimethyl*cyclo*pentanol contained about 35% of an olefin which proved to be identical with the lowest-boiling from the other isomer, and about 55% of another. The olefin common to both products was shown to be 3 : 3 : 5-trimethyl*cyclo*pentene by oxidation with potassium permanganate solution to αα*γ*-trimethylglutaric acid (m. p. and mixed m. p.). On refractionation through a 60-plate precision column it boiled at 95·2°/760 mm. (uncorr.) and had n_D^{20} 1·4160, d^{20} 0·7506, and f. p. −107·95°. The purity estimated from the freezing-point curve was 99·5 mole-%.

The second olefin from 2 : 4 : 4-trimethyl*cyclo*pentanol also possessed the 1 : 1 : 3-structure, since on subsequent hydrogenation it yielded a hydrocarbon indistinguishable from that from 3 : 5 : 5-trimethyl-*cyclo*pentene, and although on oxidation only αα-dimethylsuccinic acid was obtained, it could certainly be regarded as 1 : 4 : 4-trimethyl*cyclo*pentene. The best sample obtained, of purity estimated to be 98·8 mole-%, boiled at 103·4°/760 mm. (uncorr.) and had n_D^{20} 1·4253, d^{20} 0·7687, and f. p. −113·14°. The two remaining olefins from 2 : 2 : 4-trimethyl*cyclo*pentanol yielded on hydrogenation two isomers of 1 : 2 : 4-trimethyl*cyclo*pentane. It was therefore evident that rearrangement involving a methyl group occurs during the dehydration of this carbinol, as might have been expected from the work of Whitmore (*J. Amer. Chem. Soc.*, 1932, **54**, 3274). The two olefins were therefore regarded as isomeric 1 : 2 : 4-trimethyl*cyclo*pentenes, b. p. 111° (uncorr.), n_D^{20} 1·4308, and b. p. 118° (uncorr.), n_D^{20} 1·4390.

1 : 1 : 3- *and* 1 : 2 : 4-*Trimethyl*cyclo*pentanes.*—The samples of 3 : 5 : 5- and 1 : 4 : 4-trimethyl*cyclo*-pentene were hydrogenated separately in a high-pressure autoclave over Raney nickel. The hydrocarbon products were passed through columns of activated silica gel to remove traces of olefins and finally fractionally distilled through a 100-plate precision column. The product, which was identical from both olefins, formed a glass at its f. p. and did not crystallise. It had b. p. 104·70°/752 mm., d^{20} 0·7483, d^{25} 0·7437, n_D^{20} 1·4111, n_{5463}^{20} 1·4090, n_{4861}^{20} 1·4129, n_{4861}^{20} 1·4163, n_{4358}^{20} 1·4205, n_D^{25} 1·4087, n_{5463}^{25} 1·4066, n_{4861}^{25} 1·4106, n_{4861}^{25} 1·4138, and n_{4358}^{25} 1·4181. Rossini *et al.* (*J. Res. Nat. Bur. Stand.*, 1949, **43**, 473; 1947, **38**, 53) give b. p. 104·893°/760 mm., d^{20} 0·74825, d^{25} 0·74392, n_D^{20} 1·41119, n_D^{25} 1·40870, and f. p. −142·44°.

The higher-boiling olefins obtained from 2 : 2 : 4-trimethyl*cyclo*pentanol were treated in the same manner, and the product on distillation yielded two saturated hydrocarbons, b. p. 108·95°/751 mm., n_D^{20} 1·4106, d^{20} 0·7471, and b. p. 116·55°/751 mm., n_D^{20} 1·4184, d^{20} 0·7634. The physical properties of these hydrocarbons correspond with those of *cis-trans-cis-* and the *cis-cis-trans*-1 : 2 : 4-trimethyl*cyclo*pentanes respectively. Recently published data (Rossini *et al.*, *loc. cit.*) for these two compounds are : *cis-trans-cis*, b. p. 109·290°/760 mm., n_D^{20} 1·41060, d^{20} 0·74727; *cis-cis-trans*, b. p. 116·731°/760 mm., n_D^{20} 1·41855, d^{20} 0·76345.

Our thanks are due to the Chairman of the Anglo-Iranian Oil Company Limited for permission to publish these results. We also acknowledge the assistance of Messrs. R. A. Dean, D. T. McAllan, and J. F. Osborne in the preparative work and the late Mr. R. A. Lowry for determining the physical constants.

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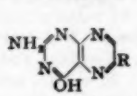
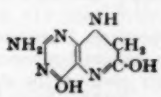
344. *Pteridines. Part III.* Unambiguous Syntheses of Xanthopterin and 2-Amino-4-hydroxy-6-methylpteridine.*

By W. R. Boon and T. Leigh.

Reduction of ethyl 2-amino-6-hydroxy-5-phenylazo-4-pyrimidylaminoacetate (V; R = OEt) gives dihydroxanthopterin (II). Similarly, reduction of 2-amino-6-hydroxy-5-phenylazo-4-pyrimidylaminoacetone (V; R = Me) and 2-amino-6-hydroxy-4-(ω-phenoxyacetonylamino)-5-phenylazopyrimidine (V; R = CH_2·OPh) gives 2-amino-7 : 8-dihydro-4-hydroxy-6-methylpteridine. The dihydro-compounds are readily oxidised to the parent pteridines.

Two of the key compounds in the study of pteridine derivatives of natural origin are xanthopterin (I; R = OH) and 2-amino-4-hydroxy-6-methylpteridine (I; R = Me). Although the structures of these two substances have been established, beyond any reasonable doubt, by degradative methods they have not hitherto been obtained synthetically by completely unequivocal methods.


(I.)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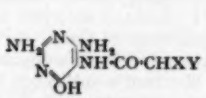
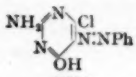

(III.)

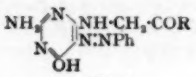
Xanthopterin has been synthesised by Purrmann (*Annalen*, 1941, **546**, 98), who condensed 2 : 4 : 5-triamino-6-hydroxypyrimidine with dichloroacetic acid to obtain the amide (III; X = Y = Cl), which when heated with silver oxide gave xanthopterin in poor yield. Koschara (*Z. physiol. Chem.*, 1943, **277**, 159) obtained a better yield by condensing the same pyrimidine with the bisulphite compound of barium glyoxylate in concentrated sulphuric acid. Both of these syntheses, at least in their structure-determining aspect, require that the initial acylation occurs on the 5-amino-group of the pyrimidine. Although this has been one of the accepted principles of pyrimidine chemistry since 1900 (Traube, *Ber.*, **33**, 3035), there was no direct proof that it was so until Wilson (*J.*, 1948, 1157) obtained 5-acetamido-2 : 4-diamino-6-hydroxypyrimidine (III; X = Y = H) by condensation of ethyl acetamidocyanoacetate with guanidine, identical with the product obtained by direct acetylation of 2 : 4 : 5-triamino-6-hydroxypyrimidine. Xanthopterin has also been obtained by oxidation of dihydroxanthopterin, to which O'Dell, Vandenbelt, Bloom, and Pfiffner (*J. Amer. Chem. Soc.*, 1947, **69**, 250) assigned the structure (II). They obtained this substance by reduction of xanthopterin; it has similarly been obtained from leucopterin (Totter, *J. Biol. Chem.*, 1944, **154**, 105; Elion, Light, and Hitchings, *J. Amer. Chem. Soc.*, 1949, **71**, 741) and xanthopterincarboxylic acid (Purrmann, *Annalen*, 1941, **548**, 284). Hitchings and Elion (*J. Amer. Chem. Soc.*, 1949, **71**, 467) have cast doubt on the assignment of structure (II) to dihydroxanthopterin by showing that the product obtained by reaction of 2 : 4-diamino-5-chloroacetamido-6-hydroxypyrimidine (III; X = H, Y = Cl) with sodium hydrogen carbonate is different from dihydroxanthopterin. Whatever may be the constitution of the substance prepared by Hitchings and Elion, we have now shown, by an extension of the methods described in Part I (Boon, Jones, and Ramage, *J.*, 1950, 96), that dihydroxanthopterin has the structure (II).

The most direct method for the preparation of dihydroxanthopterin by the above procedure would involve, initially, condensation of a glycine ester with 2-amino-4 : 6-dichloro-5-nitropyrimidine. Unfortunately, the preparation of this substance proved unexpectedly difficult and recourse was had to the use of a 4-chloro-5-phenylazopyrimidine, the phenylazo-residue serving both as a precursor of the 5-amino-group and to activate the adjacent chlorine atom. No identifiable product was isolated from the reaction of 2-amino-4 : 6-dihydroxy-5-phenylazopyrimidine with phosphorus oxychloride in dimethylaniline. The sodium salt of the pyrimidine when heated with phosphorus oxychloride gave 2-amino-6-hydroxy-5-phenylazo-4-pyrimidyl dihydrogen phosphate. Addition of phosphorus pentachloride to the reaction mixture led to formation of a product containing, in addition to phosphorus, chlorine so labile that it was readily lost on exposure to moist air.

* Part II, *J.*, 1951, 591.

In view of the failure to prepare a 4-chloro-5-phenylazopyrimidine directly from the 4-hydroxy-compound, the possibility of preparing it by coupling a suitable chloropyrimidine with a diazo-compound remained to be explored. Lythgoe, Todd, and Topham (*J.*, 1944, 315) have shown that 5-arylazopyrimidines are only obtainable when the pyrimidine is substituted at positions 2 or 4 and 6 by such groups as amino and hydroxy. 2-Amino-4-chloro-6-hydroxypyrimidine was readily obtained by acid hydrolysis of 2-amino-4-chloro-6-methoxypyrimidine (Rose and Tuey, *J.*, 1946, 81); it coupled rather slowly with benzenediazonium chloride to give 2-amino-4-chloro-6-hydroxy-5-phenylazopyrimidine (IV). This condensed readily with glycine ethyl ester in formodimethylamide solution to give ethyl 2-amino-6-hydroxy-5-phenylazo-4-pyrimidylaminoacetate (V; R = OEt), readily reduced by zinc and acetic acid to dihydroxanthopterin identical in ultra-violet absorption spectrum and *X*-ray powder photograph with an authentic specimen prepared from leucopterin (Elion *et al.*, *loc. cit.*). Oxidation with alkaline potassium permanganate by the method of Elion *et al.* converted the dihydroxanthopterin into xanthopterin.


(IV.)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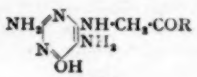
(VI.)

By hydrolysis of their "β-dihydroxanthopterin," prepared by reaction of 2 : 4-diamino-5-chloroacetamido-6-hydroxypyrimidine with sodium hydrogen carbonate, Hitchings and Elion (*loc. cit.*) obtained a substance to which they assigned the structure (VI; R = OH) and from which they prepared a methyl ester (VI; R = OMe). Both the acid and the ester were readily reconverted into β-dihydroxanthopterin. There is no doubt that the acid obtained by the above authors does not possess the structure (VI), since the ethyl ester of the acid of the above structure is shown by the present series of reactions to cyclise to dihydroxanthopterin. In an attempt to isolate a substance having the structure (VI), *iso*propyl 2-amino-6-hydroxy-5-phenylazo-4-pyrimidylaminoacetate (V; R = OPr^i) was prepared by condensation of (IV) with glycine *iso*propyl ester, since Abderhalden and Suzuki (*Z. physiol. Chem.*, 1928, **176**, 103) have shown that the latter substance only takes part sluggishly in amide-forming reactions as judged by its rate of conversion into diketopiperazine. No trace of (VI; R = OPr^i), could be isolated after reduction of (V; R = OPr^i) either in *NN*-dimethylformamide solution over Raney nickel or in *iso*propyl-alcoholic hydrochloric acid over palladised charcoal; the only product identified was dihydroxanthopterin.

2-Amino-4-hydroxy-6-methylpteridine was first obtained by Boothe, Waller, Stokstad, Hutchings, Mowat, Angier, Semb, SubbaRow, Cosulich, Fahrenbach, Hultquist, Kuh, Northey, Seeger, Sickels, and Smith (*J. Amer. Chem. Soc.*, 1948, **70**, 27) by reduction of 2-amino-4-hydroxy-6-pteridylmethylpyridinium iodide followed by oxidation of the dihydropteridine. It has since been prepared by a number of authors by condensation of 2 : 4 : 5-triamino-6-hydroxypyrimidine with suitable three-carbon compounds (cf. Angier, Waller, Boothe, Mowat, Semb, Hutchings, Stokstad, and SubbaRow, *ibid.*, p. 3029; Karrer and Schwyzer, *Helv. Chim. Acta*, 1949, **32**, 423; 1950, **33**, 39; King and Spensley, *Nature*, 1949, **164**, 574; Forrest and Waller, *J.*, 1949, 2077; Weygand, Wacker, and Schmied-Kowarzik, *Experientia*, 1950, **6**, 184). By their nature, these syntheses contain an element of uncertainty in the determination of the structure of the final product; Weygand *et al.* (*loc. cit.*) state that mixed products are always obtained, though some improvement has been claimed by Forrest and Walker (*loc. cit.*) if condensation of the pyrimidine with α-ketols is effected in presence of hydrazine.

Aminoacetone did not condense satisfactorily with (IV), but aminoacetone semicarbazone readily condensed with it in *NN*-dimethylformamide to give the semicarbazone of 2-amino-6-hydroxy-5-phenylazo-4-pyrimidylaminoacetone (V; R = Me); this substance was readily hydrolysed, without previous purification, with cold dilute hydrochloric acid to the parent ketone, which was reduced with zinc and acetic acid to 2-amino-7 : 8-dihydro-4-hydroxy-6-methylpteridine, which on oxidation with alkaline potassium permanganate gave 2-amino-4-hydroxy-6-methylpteridine.

Boothe *et al.* (*loc. cit.*) converted the last substance into 2-amino-6-bromomethyl-4-hydroxypteridine in poor yield by heating it with bromine in hydrobromic acid. It was thought that a substance such as 2-amino-4-hydroxy-6-phenoxymethylpteridine would offer a more suitable starting point for the preparation of this bromo-compound. Condensation of (IV) with the semicarbazone of 1-amino-3-phenoxypropan-2-one proceeded smoothly to give the semicarb-

azone of 2-amino-6-hydroxy-4-(ω-phenoxyacetonylamino)-5-phenylazopyrimidine (V; R = CH_2·OPh). Reduction of the parent ketone under a variety of conditions led invariably to 2-amino-7 : 8-dihydro-4-hydroxy-6-methylpteridine as the sole product. This result is almost certainly due to the splitting off of phenol from 2-amino-7 : 8-dihydro-4-hydroxy-6-phenoxymethylpteridine first formed, followed by reduction of the resultant 2-amino-4-hydroxy-6-methylpteridine. Angier *et al.* (*loc. cit.*), Weygand, Wacker, and Schmied-Kowarzik (*Experientia*, 1948, **4**, 427), and Weygand and Schmied-Kowarzik (*Ber.*, 1949, **82**, 333) have already produced evidence suggesting that 7 : 8-dihydropteridines containing the group CH_2X, where X = OH, NHR, etc., in the 6-position are unstable and capable of only a transitory existence.

1-Ethoxy- and 1-phenoxy-3-phthalimidopropan-2-ol were obtained readily by reaction of the appropriate glycidyl ethers with phthalimide. Oxidation to the ketones, with chromium trioxide in acetic acid, proceeded smoothly, but hydrolysis of the phthalimido-groups was not possible without simultaneous hydrolysis of the ether group. 1-Phenoxy-3-succinimidopropan-2-one was made by a similar series of reactions and could not be hydrolysed any more readily. The semicarbazone of 1-phenoxy-3-phthalimidopropan-2-one, however, was hydrolysed by a two-stage procedure to the semicarbazone of the amino-ketone, by use of dilute sodium hydroxide to convert the phthalimide into the phthalamic acid, which was then further hydrolysed with dilute acid.

The condensation of a 5-arylazo-4-chloropyrimidine with α-amino-ketones and esters forms the subject matter of B.P. Appl. 21,615/1949, Boon, Leigh, and Imperial Chemical Industries Limited.

Experimental.

(Microanalyses are by Drs. Weiler and Strauss.)

2-Amino-4 : 6-dihydroxy-5-phenylazopyrimidine.—To a solution of 2-amino-4 : 6-dihydroxypyrimidine (23 g.) and sodium hydrogen carbonate (45 g.) in sodium hydroxide (0·2N.; 1 l.), benzenediazonium chloride [from aniline (14 g.) and 5N-hydrochloric acid (80 c.c.)] was added during 30 minutes. After 1 hour the yellow solid was filtered off and washed with water. The filter cake was dissolved in hot N-sodium hydroxide (200 c.c.), 10N-sodium hydroxide (50 c.c.) was added, and the crystalline sodium salt which separated was collected, washed with 0·5N-sodium hydroxide, and dried *in vacuo* at 100° (33 g.). For analysis the *pyrimidine* was recrystallised from hot 2N-sodium carbonate to give a microcrystalline yellow solid, m. p. above 300° (Found: C, 51·6; H, 4·1; N, 30·1. $C_{10}H_8O_2N_4$ requires C, 52·0; H, 3·9; N, 30·3%).

2-Amino-6-hydroxy-5-phenylazo-4-pyrimidyl Dihydrogen Phosphate.—The sodium salt of 2-amino-4 : 6-dihydroxy-5-phenylazopyrimidine (5 g.) and phosphorus oxychloride were heated on a steam-bath for 4 hours. The precipitated solid was collected, washed with hot phosphorus oxychloride, and dissolved in 2% sodium hydrogen carbonate solution (100 c.c.). The pale yellow *phosphate* precipitated by addition of acetic acid had m. p. above 300° (Found: C, 38·6; H, 3·3; N, 23·0; P, 10·8. $C_{10}H_{10}O_5N_4P$ requires C, 38·6; H, 3·2; N, 22·5; P, 10·0%).

2-Amino-4-chloro-6-hydroxypyrimidine.—2-Amino-4-chloro-6-methoxypyrimidine (32 g.) and concentrated hydrochloric acid (130 c.c.) were heated on the steam-bath for 30 minutes, and the resulting suspension poured into cold water (500 c.c.). The *chloro*-compound was collected, washed with water, dried, and recrystallised from methanol; the yield was 28·5 g., 98%, and the m. p. 261° (Found: C, 32·9; H, 3·2; N, 28·7; Cl, 23·8. $C_4H_4ON_3Cl$ requires C, 33·0; H, 2·8; N, 28·9; Cl, 24·4%).

2-Amino-4-chloro-6-hydroxy-5-phenylazopyrimidine.—To a solution of the foregoing compound (87 g.) and anhydrous sodium carbonate (120 g.) in 0·2N-sodium hydroxide (3·6 l.), there was added during 1 hour a solution of benzenediazonium chloride [from aniline (56 g.) and 5N-hydrochloric acid (320 c.c.)]. After a further 12 hours' stirring, the brown precipitate was collected and washed successively with water, ethanol, and ether; the yield was 101 g., 67%. Purification of this substance for analysis proved difficult, attempts at crystallisation leading to decomposition. The *diethylamine* salt was prepared by adding diethylamine (1·0 c.c.) to a solution of the azo-compound (0·5 g.) in *NN*-dimethylformamide (8·0 c.c.); after 5 minutes the salt (m. p. 118°, decomp.) was filtered off and washed with acetone (Found: C, 51·5; H, 6·0; N, 25·0; Cl, 10·5. $C_{10}H_8ON_5Cl,C_4H_{11}N$ requires C, 52·1; H, 5·9; N, 26·1; Cl, 11·0%). This substance likewise could not be purified further without decomposition. If the salt is not removed rapidly from the reaction mixture, it redissolves with the formation of *2-amino-4-diethylamino-6-hydroxy-5-phenylazopyrimidine*, m. p. 206°, isolated by addition of water and recrystallised from ethanol (Found: C, 59·0; H, 6·4; N, 29·9. $C_{14}H_{18}ON_6$ requires C, 58·7; H, 6·3; N, 29·4%).

Ethyl 2-Amino-6-hydroxy-5-phenylazo-4-pyrimidylaminoacetate.—To 2-amino-6-chloro-4-hydroxy-5-phenylazopyrimidine (1 g.) in dimethylformamide (5 c.c.), glycine ethyl ester (0·9 g.) in ethanol (10 c.c.) was added. Next day, the *ester* was filtered off, washed with ethanol and water, dried, and recrystallised from n-butanol; it had m. p. 238° (1·1 g.; 85%) (Found: C, 53·4; H, 5·2; N, 27·0. $C_{14}H_{16}O_3N_6$ requires C, 53·2; H, 5·1; N, 26·6%). The corresponding *isopropyl* ester (Found: C, 54·1; H, 5·4; N, 25·4. $C_{15}H_{18}O_3N_6$ requires C, 54·5; H, 5·5; N, 25·4%) was obtained similarly by using an *iso*propanol solution of glycine *iso*propyl ester; recrystallised from *iso*propanol, it had m. p. 222°.

Dihydroxanthopterin.—To ethyl 2-amino-6-hydroxy-5-phenylazo-4-pyrimidylaminoacetate (1·0 g.) in glacial acetic acid (10 c.c.), heated to 90°, zinc dust (1 g.) was added with stirring during 10 minutes. After being decanted from most of the unused zinc dust, the reaction mixture was centrifuged, and the solid crystallised from 0·25N-sulphuric acid as the *sulphate dihydrate* (0·6 g.) [Found, on sample dried at

90°/0·5 mm.: C, 29·4; H, 3·9; N, 28·4; S, 6·4. $(C_4H_7O_2N_3)_2,H_2SO_4,2H_2O$ requires C, 29·0; H, 4·0; N, 28·2; S, 6·5%]. The ultra-violet absorption in 0·1N-hydrochloric acid and the *X*-ray powder photograph of the free base were identical with those of an authentic sample prepared by reduction of leucopterin (Elion *et al.*, *loc. cit.*). It was readily converted into xanthopterin by oxidation with alkaline potassium permanganate as described by Elion *et al.*

Aminoacetone Semicarbazone.—To aminoacetone hydrochloride (38 g.) in ethanol (250 c.c.), semicarbazide hydrochloride (48 g.) in water (100 c.c.) was added. After 2 hours, *aminoacetone semicarbazone hydrochloride* (53 g., 87%) was collected, washed with ethanol, and crystallised from aqueous ethanol; it had m. p. 212° (Found: C, 29·1; H, 6·7; N, 34·1; Cl, 21·9. $C_4H_{11}ON_4Cl$ requires C, 28·8; H, 6·6; N, 33·6; Cl, 21·3%).

1-*Ethoxy*-3-*phthalimidopropan*-2-*ol.*—Glycidyl ethyl ether (Fairbourne, Gibson, and Stephens *J.*, 1932, 1965) (262 g.) and phthalimide (370 g.) were heated at 150° for 24 hours. After distillation of unchanged ether (71 g.), benzene (1 l.) was added, and phthalimide (99 g.) removed by filtration. Concentration of the filtrate gave 1-*ethoxy*-3-*phthalimidopropan*-2-*ol* (350 g., 75%), m. p. 68° (Found: C, 63·0; H, 6·1; N, 6·0. $C_{13}H_{15}O_4N$ requires C, 62·7; H, 6·0; N, 5·6%).

1-*Phenoxy*-3-*phthalimidopropan*-2-*ol*, m. p. 117°, from ethanol (Found: C, 68·7; H, 5·1; N, 4·4. $C_{17}H_{15}O_4N$ requires C, 68·6; H, 5·0; N, 4·7%), and 1-*phenoxy*-3-*succinimidopropan*-2-*ol*, m. p. 132°, from ethanol (Found: C, 62·4; H, 5·8; N, 5·4. $C_{13}H_{15}O_4N$ requires C, 62·5; H, 6·0; N, 5·6%), were obtained similarly.

1-*Ethoxy*-3-*phthalimidopropan*-2-*one.*—To a solution of 1-ethoxy-3-phthalimidopropan-2-ol (25 g.) in glacial acetic acid (100 c.c.) warmed to 30°, 21 c.c. of a 5·75M-solution of chromium trioxide in 50% acetic acid were added in portions during 45 minutes. After a further 30 minutes' heating on the steam-bath, the acetic acid was removed under reduced pressure, and the residue was triturated with water and extracted with ether. The ethereal solution was washed with sodium hydrogen carbonate solution and dried ($MgSO_4$), and the ether removed by distillation. The semi-solid residue was twice crystallised from aqueous methanol, and 1-*ethoxy*-3-*phthalimidopropan*-2-*one* was obtained, having m. p. 75° (Found: C, 62·9; H, 5·2; N, 5·4. $C_{13}H_{13}O_4N$ requires C, 63·1; H, 5·3; N, 5·7%); the 2 : 4-*dinitrophenylhydrazone* had m. p. 224° (Found: C, 52·8; H, 3·8; N, 16·3. $C_{19}H_{17}O_7N_5$ requires C, 53·4; H, 4·0; N, 16·4%). 1-*Phenoxy*-3-*phthalimidopropan*-2-*one*, recrystallised from ethanol, had m. p. 164° (Found: C, 69·0; H, 4·4; N, 4·7. $C_{17}H_{13}O_4N$ requires C, 69·1; H, 4·4; N, 4·7%) [*semicarbazone* (from *n*-butanol), m. p. 193° (Found: C, 61·6; H, 4·9. $C_{18}H_{16}O_4N_4$ requires C, 61·4; H, 4·6%], and 1-*phenoxy*-3-*succinimidopropan*-2-*one*, m. p. 112° (from methanol) (Found: C, 63·2; H, 5·4; N, 5·9. $C_{13}H_{13}O_4N$ requires C, 63·1; H, 5·3; N, 5·7%), were obtained similarly.

1-*Amino*-3-*phenoxypropan*-2-*one Semicarbazone.*—Sodium hydroxide (13 g.) in water (200 c.c.) was added during 15 minutes with stirring to a suspension of 1-phenoxy-3-phthalimidopropan-2-one semicarbazone (98 g.) in ethanol (500 c.c.). After 1 hour, the solution was filtered, and the bulk of the ethanol removed by distillation under reduced pressure. The solution was cooled to 5°, concentrated hydrochloric acid (40 c.c.) added, and the *phthalamic acid* (1-*o*-*carboxybenzamido*-3-*phenoxypropan*-2-*one semicarbazone*) filtered off, washed with water, and air-dried. A sample, redissolved in sodium hydroxide, treated with charcoal, filtered, and reprecipitated, had m. p. 135° (Found: N, 14·5. $C_{18}H_{19}O_5N_4$ requires N, 15·1%). The phthalamic acid (87 g.), ethanol (250 c.c.), and 0·33N-hydrochloric acid (120 c.c.) were heated on the steam-bath for 30 minutes. The syrupy residue, obtained on evaporation to dryness under reduced pressure, was lixiviated with water (200 c.c.), filtered to remove phthalic acid, and the filtrate again evaporated to dryness. The residue was dissolved in hot ethanol (250 c.c.) from which on cooling there was obtained 1-*amino*-3-*phenoxypropan*-2-*one semicarbazone hydrochloride* (23 g., 31%), m. p. 194°, raised to 201° by recrystallisation from ethanol (Found: C, 45·9; H, 6·3; N, 22·0. $C_{10}H_{15}O_2N_4Cl$ requires C, 46·4; H, 5·8; N, 21·7%).

2-*Amino*-6-*hydroxy*-5-*phenylazo*-4-*pyrimidylaminoacetone.*—Aminoacetone semicarbazone hydrochloride (107 g.) was added to a cold solution of sodium ethoxide [from sodium (14·8 g.) and ethanol (600 c.c.)]. After 2 hours the mixture was added to 2-amino-4-chloro-6-hydroxy-5-phenylazopyrimidine (75 g.) in dimethylformamide (400 c.c.). Next day, the solid was collected, washed successively with ethanol and water, and dried in air. The semicarbazone (88 g.) was dissolved in glacial acetic acid (250 c.c.), and 2N-hydrochloric acid (1500 c.c.) added. 2-*Amino*-6-*hydroxy*-4-*acetonylamino*-5-*phenylazopyrimidine hydrochloride* (75 g., 76%), m. p. >300°, separated in a few minutes; it was filtered off, and washed with 0·5N-hydrochloric acid and then with acetone (Found: C, 48·4; H, 5·1; N, 25·4; Cl, 10·8. $C_{13}H_{15}O_3N_6Cl$ requires C, 48·4; H, 4·7; N, 26·0; Cl, 11·0%). The free base (from ethanol) had m. p. 183°.

2-*Amino*-6-*hydroxy*-4-(ω-*phenoxyacetonylamino*)-5-*phenylazopyrimidine hydrochloride*, m. p. 192° (from methanol) (Found: C, 54·9; H, 4·7; N, 20·1; Cl, 8·5. $C_{19}H_{19}O_3N_6Cl$ requires C, 55·0; H, 4·6; N, 20·3; Cl, 8·6%), and its *semicarbazone*, m. p. 265° (decomp.) (from dimethylformamide–ethanol) (Found: C, 54·9; H, 4·7; N, 29·0. $C_{20}H_{21}O_3N_9$ requires C, 55·2; H, 4·8; N, 29·0%), were obtained similarly.

2-*Amino*-7 : 8-*dihydro*-4-*hydroxy*-6-*methylpteridine.*—To a stirred solution of 2-amino-6-hydroxy-5-phenylazo-4-pyrimidylaminoacetone hydrochloride (51 g.) i glacial acetic acid (250 c.c.) at 90°, zinc dust (40 g.) was added during 30 minutes. The mixture was filtered hot, and 5N-hydrochloric acid (500 c.c.) added to the filtrate. The solid which separated was collected after 30 minutes, washed with 2N-hydrochloric acid, and dissolved in 0·25N-sodium hydroxide (1 l.) at 60°, and the solution filtered. Concentrated hydrochloric acid (150 c.c.) was added to the filtrate to give 2-amino-7 : 8-dihydro-4-hydroxy-6-methylpteridine hydrochloride (25 g.), m. p. >300°. A sample for analysis was dried over phosphoric oxide at 100°/0·5 mm. (Found: C, 35·7; H, 5·1; N, 30·4; Cl, 15·2. Calc. for $C_7H_9ON_5,HCl,H_2O$: C, 36·0; H, 5·1; N, 30·0; Cl, 15·3%). The ultra-violet absorption in 0·1N-sodium hydroxide and an *X*-ray powder photograph were identical with those of a sample prepared by the

method of Boothe *et al.* (*loc. cit.*). Oxidation with alkaline permanganate readily converted the product into 2-amino-4-hydroxy-6-methylpteridine. The dihydro-compound was also obtained by reduction of 2-amino-6-hydroxy-4-(ω-phenoxyacetonylamino)-5-phenylazopyrimidine hydrochloride with zinc dust in acetic acid at room temperature, of the free base (i) similarly at 90°, (ii) with hydrogen and Raney nickel in ethanol at 50°, or (iii) with boiling sodium dithionite solution.

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345. *Unsaturated Lactones and Related Substances. Part V.* Dihydro-β-ketomuconic Acid and Carboxy-lactones of the Protoanemonin Type.*

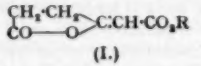
By ULLI EISNER, J. A. ELVIDGE, and R. P. LINSTEAD.

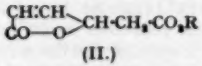
The investigation of the chemistry of unsaturated lactonic acids of potential biological activity has been continued.

Fumaric half-ethyl ester half-chloride (made by a very convenient process from maleic anhydride) reacts with ethyl magnesiomalonate to yield ethyl *trans*-β-carbethoxyacrylylmalonate (VII*a*), characterised as the copper enolate. β-Carbomethoxyacrylyl chloride with ethyl and methyl magnesiomalonates similarly affords the triesters (XI) and (VII; R = R′ = Me), which like (VII*a*) give only poor yields of dihydro-β-ketomuconic acid (XV) on hydrolysis, cleavage products (fumaric and malonic acids) predominating. The course of this and related hydrolyses is discussed. Cyclodehydration of (XV) with acetic anhydride–hydrogen bromide affords in very low yield the lactonic acid (III; R = H), converted by diazoethane into the ethyl ester (III; R = Et). The latter arose, as well as γ-dicarbethoxymethylenebutenolide (IV), by pyrolysis of (VII*a*). (IV) is best prepared by cyclisation of ethyl *trans*-β-carboxyacrylylmalonate (XIII), obtained from (VII*a*) with ethanolic potassium hydroxide. The lactone (IV) is comparatively stable to water, and lacks reducing properties, but is readily cleaved to maleic acid and ethyl malonate by aqueous alkali. Hydrogenation affords only the deoxy-acid: no saturated lactone or partial-reduction products were obtained. (IV) is ring-opened to ethyl *trans*-β-anilidoacrylylmalonate (XXIV) by aniline, to (VII*a*) with ethanolic hydrogen chloride, but to the corresponding *cis*-ester (VII*b*) by ethanolic sodium ethoxide, a finding of significance in relation to previous studies in the muconic series.

During the work αβ-dibromo-β′-ketoadipic acid (XVIII) was obtained and cyclised to an unsaturated bromo-lactone (XX).

IN preceding papers of this series attention has been directed to those properties of simple unsaturated lactones which indicate the position of the double bond. Thus in Parts III and IV (Eisner, Elvidge, and Linstead, *J.*, 1950, 2223; Elvidge, Linstead, Orkin, Sims, Baer, and Pattison, *ibid.*, p. 2228) the marked differences in the behaviour between the isomeric γ-lactones (I) and (II) on reduction and treatment with certain reagents were discussed. The corresponding doubly-unsaturated γ-lactone system has now been synthesised. This is exemplified by the compounds (III) and (IV), which combine the structural features of both the simpler lactones (I) and (II).


(I.)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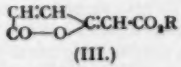
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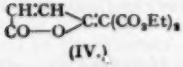
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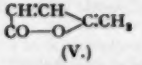
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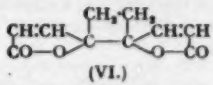
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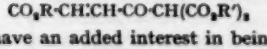

(VII.)

The lactones (III) and (IV) have an added interest in being derivatives of protoanemonin (V), the γ-lactone of β-acetylacrylic acid. Protoanemonin (for bibliography, see Haynes, *Quart. Reviews*, 1948, **2**, 46) is one of the simplest unsaturated lactones possessed of any marked

* Part IV, *J.*, 1950, 2228.

antibiotic activity, and operates against a surpisingly wide variety of bacteria. It polymerises quite rapidly, however, mainly to the dimer, anemonin (VI), which has only a feeble antibacterial action. A few other compounds containing the protoanemonin system are known, *e.g.*, the halogen-substituted analogues prepared by Karrer and his co-workers (*Helv. Chim. Acta*, 1947, **30**, 859; 1949, **32**, 1019, 1028), and methylenephthalide and its derivatives.

The ready preparation of γ-carboxymethylenebutanolide (I; R = H) by the cyclodehydration of β-ketoadipic acid (Eisner, Elvidge, and Linstead, *loc. cit.*) suggested that γ-carboxymethylenebutenolide (III; R = H) might be obtained similarly from the *unsaturated* keto-acid, dihydro-β-ketomuconic acid.

An investigation of the synthesis of this unknown acid was accordingly undertaken first. An obvious route was the reaction of a half-ester half-chloride of fumaric acid with magnesiomalonic ester to give the triester (VII), followed by hydrolysis and mono-decarboxylation. The subsidiary problems which arose are conveniently considered under the following headings.

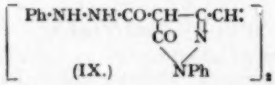
(a) *β-Carbalkoxyacrylyl Chlorides.*—The half-methyl ester half-chloride of fumaric acid (β-carbomethoxyacrylyl chloride) has been prepared from fumaryl chloride and methanol (Lutz, *J. Amer. Chem. Soc.*, 1930, **52**, 3423), but the product is difficult to separate and purify because of its tendency to co-distil with the unchanged dichloride and with the diester which is also formed. A preparation from methyl fumarate, involving hydrolysis to methyl hydrogen fumarate and reaction of the latter with thionyl chloride (Erlenmeyer and Schoenauer, *Helv. Chim. Acta*, 1937, **20**, 1008), proved very tedious and, on a reasonably large scale, virtually unworkable because of the conditions of extreme dilution necessary for half-hydrolysis of the ester (Waren and Grose, *J. Amer. Chem. Soc.*, 1912, **34**, 1600; Erlenmeyer and Schoenauer, *loc. cit.*) and the labour of isolating and drying the product. Moreover, the β-carbomethoxyacrylyl chloride which was eventually obtained by this process was not pure. The main product, m. p. 54°, from the reaction with ethyl magnesiomalonate was contaminated with methyl fumarate, which was difficult to remove, and a very sparingly soluble substance, m. p. 117°, was also present.

Attention was then turned to a possible shorter route which might have led to desirable *cis*-material. Maleic half-ester was allowed to react with thionyl chloride under conditions analogous to those for the corresponding succinic acid derivatives (Riegel and Lilienfeld, *J. Amer. Chem. Soc.*, 1945, **67**, 1273), but fractional distillation failed to afford any sharp separation of the products. A portion of the first runnings reacted with *p*-aminobenzenesulphonamide to yield the half " sulphanilamide " of ethyl fumarate, and a later fraction gave a chlorine-containing derivative, $C_{18}H_{15}O_5N_4ClS$, which obviously differed from both the known half-sulphanilamide half-ethyl esters of maleic and fumaric acids (Bergmann and Schapiro, *J. Org. Chem.*, 1942, **7**, 419). The formation from maleic half-ester and thionyl chloride of a hydrogen chloride addition product (mixed chlorosuccinic half-ester chlorides), as well as fumaric half-ester chloride, which is indicated by these results, contrasts strongly with the straightforward formation of the latter from fumaric half-ester and thionyl chloride. Maleic half-ester half-chlorides have not been reported hitherto, though maleyl chloride (which has a cyclic structure) can be prepared in small quantities (Ott, *Annalen*, 1912, **392**, 245; van Dorp and van Dorp, *Rec. Trav. chim.*, 1906, **25**, 96; Anschütz and Wirtz, *Ber.*, 1885, **18**, 1947).

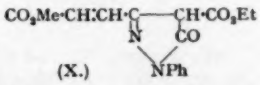
Eventually a reproducible and highly convenient method for β-carbethoxyacrylyl chloride was devised. When maleic anhydride was dissolved in 1 mol. of hot ethanol and a small quantity of thionyl chloride then added, ethyl hydrogen fumarate was readily obtained in good yield, and from it with thionyl chloride pure β-carbethoxyacrylyl chloride was easily prepared.

Repetition of this procedure with methanol gave a somewhat different result. The product from the first stage was mainly methyl fumarate, mixed with some methyl hydrogen fumarate and fumaric acid. Nevertheless, the half-ester could readily be separated in a pure state, though only in 16% overall yield. In spite of this the method was considerably more rapid and convenient, especially on a large scale, than the half-hydrolysis of methyl fumarate. Subsequent treatment of the half-ester with thionyl chloride afforded pure β-carbomethoxyacrylyl chloride in high yield.

$[(CO_2Et)_2CH{\cdot}CO{\cdot}CH{:}]_2$ (VIII.)



(IX.)

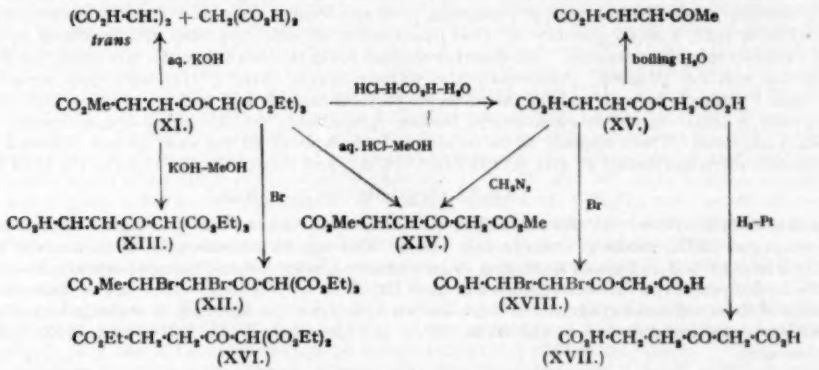


(X.)

(b) *Dihydro-β-ketomuconic Acid, Precursors, and Derivatives.*—The by-product, m. p. 117°, from the reaction (mentioned above) of slightly impure β-carbomethoxyacrylyl chloride with

ethyl magnesiomalonate was identified as the tetraethyl ester (VIII) (*trans*-1 : 1 : 6 : 6-tetracarbethoxyhex-3-ene-2 : 5-dione) by its synthesis from fumaryl chloride and 2 mols. of the malonate, and was further characterised by condensation with phenylhydrazine (of which 4 mols. reacted) to yield the high-melting derivative (IX).

The main product, m. p. 54°, from the β-carbomethoxyacrylyl chloride reaction was the expected triester (XI) (ethyl *trans*-β-carbomethoxyacrylylmalonate), which yielded a normal phenylpyrazolone derivative (X). The constitution of the ester as (XI) was confirmed by its behaviour under a variety of reaction conditions, summarised in the accompanying scheme. Cold aqueous potassium hydroxide gave a mixture of fumaric and malonic acids. With bromine, a dibromo-adduct (XII) was formed. Cold methanolic potassium hydroxide afforded the mono-acid (XIII) (ethyl *trans*-β-carboxyacrylylmalonate), and methanolic hydrogen chloride ontaining water gave the dimethyl ester (XIV), also prepared from dihydro-β-ketomuconic cid (XV) (below) and diazomethane.



Meanwhile, the possibility of hydrolysing the triester (XI) to dihydro-β-ketomuconic acid (XV) was examined. In the analogous case of the saturated compounds (Eisner, Elvidge, and Linstead, *loc. cit.*), the triester (XVI) had been smoothly hydrolysed and monodecarboxylated to the ketodicarboxylic acid (XVII) by cold concentrated hydrochloric acid. Acid hydrolysis of the new unsaturated triester (XI), however, was very difficult because of its insolubility and the relative ease of fission of the molecule to fumaric and malonic fragments. Hydrolysis of (XI) with alkali was therefore tried under conditions additional to those already described. With barium hydroxide (cf. Hunsdiecker and Hunsdiecker, *Ber.*, 1942, **75**, 291) and methanolic lithium hydroxide, only mixtures of fumaric and malonic acids resulted, together with a little partially hydrolysed ester (XIII) in the last case.

However, in acetic or formic acid solution containing water and saturated with hydrogen chloride, hydrolysis of the triester (XI) proceeded slowly, and during 2—6 days a white solid separated, which was a mixture of fumaric and dihydro-β-ketomuconic acids. The proportions, as well as the total yield, varied widely in a series of experiments. From such mixtures, provided its proportion was not too high, fumaric acid could be extracted with boiling acetone to leave in small quantity dihydro-β-ketomuconic acid (*trans*-3-ketobut-1-ene-1 : 4-dicarboxylic acid) (XV), obtained as a micro-crystalline powder, m. p. 164°, which gave a deep purple with ferric chloride, and was sparingly soluble in most organic solvents. The constitution (XV) was proved by decarboxylation of the acid in boiling water to β-acetylacrylic acid, and hydrogenation to β-ketoadipic acid (XVII) which was further characterised by conversion into lævulic acid semicarbazone. The yield of β-ketoadipic acid was low (20%) and the oil which accompanied it could not be characterised. This result is analogous to the behaviour of oxalo-crotonic and -sorbic esters on catalytic reduction (Borsche and Manteuffel, *Ber.*, 1932, **65**, 868). It was verified that β-ketoadipic acid was not reduced under the conditions employed.

With bromine in acetic acid, (XV) afforded the dibromo-adduct (XVIII). An attempt to obtain the latter by hydrolysis of the dibromo-triester (XII) with hydrobromic acid was unsuccessful, the ester being recovered unchanged. This resistance of the dibromo-triester (XII) to hydrolysis contrasts with the ease of hydrolysis of its dihydro-analogue (XVI), and may

well be due to its insolubility. Both dibromo-compounds (XII) and (XVIII) were crystalline and had every appearance of being single racemates. Indeed, this was to be expected from theoretical considerations, which indicate that each compound has purely an *erythro*-spatial arrangement of the bromine substituents, having resulted from a *trans*-addition to a double bond about which the configuration is *trans* (see literature summary by Raphael, *J.*, 1949, S 44).

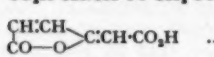
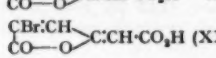
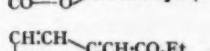
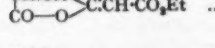
The solid trimethyl and liquid triethyl esters (VII; R = R′ = Me and Et), prepared from the appropriate fumaric half-ester chlorides and magnesiomalonates, were employed, as well as the mono-acid (XIII), in further hydrolysis experiments towards dihydro-β-ketomuconic acid (XV), but these compounds offered no advantage. For example, only 16% yields of (XV) were obtained from the trimethyl ester. Nevertheless, advantages appeared in other directions. Thus the triethyl ester (VII; R = R′ = Et) proved to be much more accessible than the other triesters, and it could be hydrolysed to the mono-acid (XIII) in over 90% yield, a reaction which, incidentally, confirmed its structure.

Hydrolysis of the tetracarboxylic ester (VIII) was also briefly studied, in view of its ready availability. The results were unpromising, although from a trans-esterification reaction with propionic acid, a small quantity of ethyl β-acetylacrylate was separated and identified as the 2 : 4-dinitrophenylhydrazone. No diacetylethylene could be detected in the non-acidic fraction of the reaction product. Apparently the tetracarboxylic ester (VIII) undergoes so-called " acid " cleavage at both ends of the molecule to yield fumaric and malonic entities, and there is only a small degree of mono-fission leading (presumably via dihydro-β-ketomuconate) to acetylacrylate. There appears to be no simple hydrolysis of all the ester groups followed by malonic decarboxylation to give $(CO_2H{\cdot}CH_2{\cdot}CO{\cdot}CH{:})_2$ and thence $CO_2H{\cdot}CH_2{\cdot}CO{\cdot}CH{:}CH{\cdot}COMe$

$$[(CO_2Et)_2CH{\cdot}CO{\cdot}CH{:}CH{\cdot}]_2 \qquad \text{(XIX.)}$$

and diacetylethylene. In this connection it is of interest to note that the higher unsaturated homologue (XIX) seems to undergo *only* " acid " cleavage to muconic acid, at least under the conditions of acid and alkali treatment so far examined, since ketonic material was absent from the hydrolysates (private communication from Dr. B. C. L. Weedon). Thus the various esters studied show a distinct gradation in behaviour on hydrolysis, the tendency to cleavage increasing with growing unsaturation in the series (XVI) (no cleavage), (VII), (VIII), and (XIX) (only cleavage).

Light-absorption characteristics (in dioxan).

Compound.	$\lambda_{max.}$, A.	ε.
$CO_2Me{\cdot}CH{:}CH{\cdot}CO{\cdot}CH(CO_2Me)_2$	3040	15,300
$CO_2H{\cdot}CH{:}CH{\cdot}CO{\cdot}CH(CO_2Et)_2$	2980	12,900
	3060	14,200
$CO_2H{\cdot}CH{:}CH{\cdot}CO{\cdot}CH_2{\cdot}CO_2H$	2280	9,160
	2980	14,200
	2580	12,200
	2700	14,000
	2810	16,200
 (XX.)	2880	19,000
	2510	7,220
	2690	12,900
	2800	14,300
	2870	12,900
	2500	9,600
	2810	17,300
	2900	17,300
$(CO_2Et)_2CH{\cdot}CO{\cdot}CH{:}CH{\cdot}CO{\cdot}CH(CO_2Et)_2$	3400	28,000

None of the unsaturated keto-esters and acids mentioned above formed carbonyl derivatives readily. The esters were strong pseudo-acids, soluble in aqueous sodium hydrogen carbonate, and, like the acids, gave deep colorations with ferric chloride. They showed ultra-violet light absorption characteristics (see Table) in keeping with the enolic forms of the formal keto-structures shown above. Characterisation of the liquid triethyl ester (VII; R = R′ = Et) was accomplished by formation of the copper enolate, $(C_{13}H_{17}O_7)_2Cu$, a beautifully crystalline green substance with m. p. 159°.

(c) *Lactones.*—First attempts to lactonise dihydro-β-ketomuconic acid (XV) with acetyl chloride, in the cold or by heating, and with ultra-violet irradiation, afforded only syrups, possibly of acid chlorides and mixed anhydrides, which on exposure to the air gradually reverted to the solid starting material. By the use of hot acetic anhydride–acetic acid in the presence of

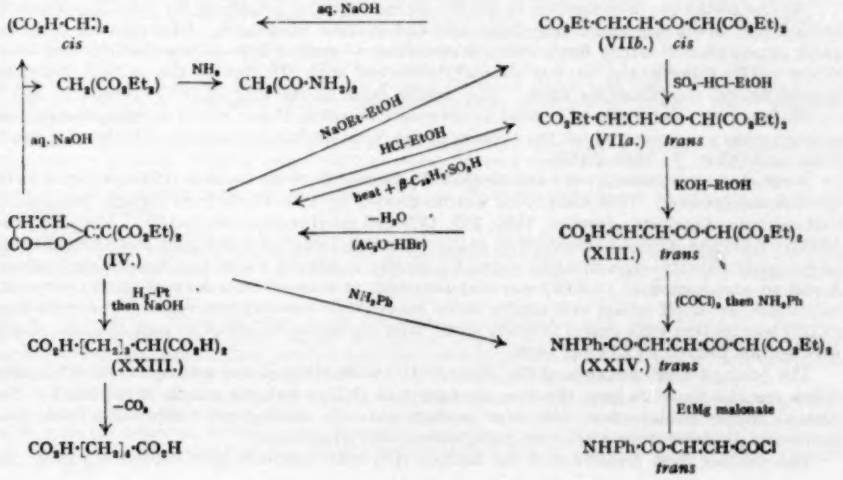
anhydrous hydrogen bromide [to permit inversion of the double bond of (XV)], a mixture of substances resulted from which a small quantity of an acid, m. p. 156°, was isolated. This gave no ferric chloride colour, gave analytical results expected for the lactonic acid (III; R = H) (γ-carboxymethylenebutenolide), $C_6H_4O_4$, and showed light-absorption properties consistent with that structure (see Table). In view of the very poor yield of lactonic product, cyclodehydration of the dibromo-keto-acid (XVIII) was examined, and found to proceed readily with acetyl chloride, as expected for a saturated γ-keto-acid. The product, however, was not the expected dibromo-lactonic acid from which (III; R = H) might have been derived by treatment with magnesium or zinc. It had the composition $C_6H_3O_4Br$ and was therefore a bromo-substituted derivative of (III; R = H), evidently formed by loss of hydrogen bromide from the initial product of cyclodehydration. Structure (XX) for the product seems probable and is consistent with the observed ultra-violet absorption spectrum (Table).

$$CO_2R{\cdot}CH{:}CH{\cdot}CO{\cdot}CH_2{\cdot}CO_2R' \qquad \text{(XXI.)}$$

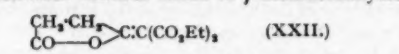
It appeared at this stage, particularly in view of the inaccessibility of dihydro-β-ketomuconic acid, that the required type of doubly-unsaturated γ-lactone might best be obtained in sufficient quantities for chemical study by cyclodehydration of the acid esters (XXI; R = H, R′ = Et) and (XIII), of which the latter was readily available. An attempt to obtain the former led to an unexpected result. It was proposed to pyrolyse the triethyl ester (VII; R = R′ = Et) to the diester (XXI; R = R′ = Et) and then to half-hydrolyse this to (XXI; R = H, R′ = Et). Application of Riegel and Lilienfeld's pyrolytic decarbethoxylation conditions (*loc cit.*) to the triester (VII; R = R′ = Et) produced a complex mixture, difficult to separate by fractionation, but from which small yields of two neutral products, m. p. 62° and 78°, were isolated, neither of which gave a ferric chloride colour. The latter compound, $C_6H_8O_4$, was γ-carbethoxymethylenebutenolide (III; R = Et). This was shown by the ultra-violet absorption spectrum (Table) and by its preparation from the lactonic acid (III; R = H) and diazoethane.

Acetic anhydride–hydrogen bromide converted the readily accessible acid ester (XIII) in good yield into the expected lactonic diester (IV) (γ-dicarbethoxymethylenebutenolide). The compound melted at 62° and was identical with the substance already obtained from the pyrolysis of the ester (VII; R = R′ = Et). It was neutral, and had the molecular formula $C_{11}H_{12}O_6$, and the ultra-violet absorption characteristics recorded in the Table.

Attempts to convert the lactonic diester (IV) into the mono-ester (III; R = Et) showed that the ester groups were extremely stable. This is generally to be expected for esters of the type $C{:}C(CO_2R)_2$. Pyrolysis with naphthalene-β-sulphonic acid, following the method of Riegel and Lilienfeld (*loc. cit.*) for malonic esters, and attempted trans-esterification with propionic acid failed. Other methods for the removal of an ester group were not applicable, as will be apparent from the reactions of the lactone (IV) described below.



As expected, none of the substituted protoanemonins described in this paper exhibited the tendency towards ready polymerisation of the parent compound (V). In many of its reactions the doubly-unsaturated ($\Delta^{\alpha\gamma}$-) lactone (IV) behaved like the γ-unsaturated γ-lactone (I), previously studied by Eisner, Elvidge, and Linstead (*loc. cit.*), but in being more stable to water it resembled (II) (Elvidge, Linstead, Orkin, Sims, Baer, and Pattison, *loc. cit.*). Unlike the simpler lactones (I) and (II), the new material (IV) showed no reducing properties. The Légal test was negative, and ammoniacal silver nitrate and dichlorophenol-indophenol were unaffected. Towards aqueous alkali, however, it was unexpectedly labile, and with very dilute sodium hydroxide in aqueous dioxan was readily cleaved in high yield to maleic acid and ethyl malonate : the former product was isolated, and further characterised by conversion into the anhydride, and the latter was converted to the solid diamide. The expected ethyl β-carboxyacrylylmalonate was not obtained. In view of the comparative stability of this keto-acid towards dilute aqueous alkali, at least when in the *trans*-form (XIII), it appears that the elimination of the side chain proceeds direct and not *via* an acyclic hydrolysis product. This interesting reaction is paralleled by the behaviour towards alkali of γ-dicarbethoxymethylenebutanolide



(XXII.)

(XXII) (Ruggli and Maeder, *Helv. Chim. Acta*, 1943, **26**, 1476), and of phthalylidenemalonic ester (Wislicenus, *Annalen*, 1887, **242**, 23). It is particularly significant that the latter reaction yields phthalic *anhydride*. This indicates the primary reaction in these fissions.

Hydrogenation of the lactonic ester (IV) in the presence of platinum resulted in an uptake of 3 mols. of hydrogen and an oily acid was formed, which did not give a ferric chloride colour. Hydrolysis of the oil afforded crystalline α-carboxyadipic acid (XXIII), decarboxylated to adipic acid when heated. 50% Hydrogenation of (IV) and separation of the resulting mixture into acidic and neutral fractions showed that no mono-unsaturated lactone [*e.g.*, (XXII)] was formed. Hydrolysis and decarboxylation of the acid fraction gave only adipic acid, and the neutral fraction was identified as the starting material (IV). Neither fraction gave a ferric chloride colour, which again shows the absence of any ketonic product. The behaviour on reduction of the unsaturated system present in (IV) thus falls into line with that of the γ-unsaturated lactone (I) (Eisner, Elvidge, and Linstead, *loc. cit.*), and with that of (XXII) (Ruggli and Maeder, *loc. cit.*). All of these compounds resemble the simple $\beta\gamma$-unsaturated γ-lactones studied by Jacobs and Scott (*J. Biol. Chem.*, 1930, **87**, 601; 1931, **93**, 139) in their complete conversion into deoxy-acid. There does not seem to be any preferential hydrogenation of the exocyclic double bond of (IV). The first stage of the process may be either αβ- or αδ-addition of hydrogen to the $\Delta^{\alpha\gamma}$-butenolide system. Further reduction of the respective possible intermediate Δ^{γ}- or Δ^{β}-lactones would in each case be expected to give the deoxy-acid as end product : the rates of these second stages must be at least as rapid as the first.

We completed our investigation of the $\Delta^{\alpha\gamma}$-lactone (IV) by examining its behaviour towards aniline, and to ethanol under anhydrous acid and alkaline conditions. Ring-opening occurred (with appearance of strong ferric chloride reactions) to yield a keto-anilide (XXIV) and keto-esters (VII), respectively, as was similarly observed with (I), but in the present reactions stereochemical complications arose. The double bond in the ring of (IV) necessarily had a *cis*-configuration, and it was of interest to determine in which, if any, of the acyclic products this configuration was preserved [cf. the opening of the mono-olefinic lactone (II), Elvidge, Linstead, Sims, and Orkin, *J.*, 1950, 2235].

Somewhat unexpectedly, the anilide (XXIV) formed from the lactone (IV) was found to be the *trans*-compound. This was proved unambiguously by a synthesis from fumaric half-anilide half-chloride (Anschütz, *Annalen*, 1890, **259**, 137) and ethyl magnesiomalonate. Moreover, the product from the lactone underwent no change in ethanol solution containing hydrogen chloride and sulphur dioxide—agents which normally readily transform maleic into fumaric derivatives. A second preparation of (XXIV) was also achieved, of interest from a synthetical viewpoint, but which by itself would not rigidly have proved the *trans*-configuration. The *trans*-acid (XIII) was treated with oxalyl chloride under mild conditions to afford an acid chloride, which with aniline formed (XXIV) at once.

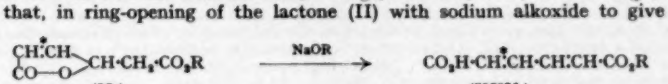
The product from reaction of the lactone (IV) with ethanol and hydrogen chloride under reflux was also found to have the *trans*-configuration (VII*a*), but this was to be expected. The derived copper enolate from the ester product gave no melting-point depression with that previously prepared from ethyl *trans*-β-carbethoxyacrylylmalonate.

The product from treatment of the lactone (IV) with cold ethanolic sodium ethoxide was

likewise (from its superficial properties) an oily keto-ester. It gave a copper enolate which existed in two forms, green needles, melting at 55° and 101° severally. These are probably polymorphs or else represent different states of solvation. Their interconversion is described in the experimental section. Neither is identical with the copper enolate of the *trans*-isomeride, m. p. 159°.

Proof that the product from the lactone (IV) and sodium ethoxide was indeed the *cis*-keto-ester (VII*b*) was finally obtained in two ways. First, with cold aqueous alkali the ester was cleaved to maleic acid, and no fumaric acid (which would have been readily apparent) could be detected. Secondly, after treatment of the ester in ethanol with hydrogen chloride and sulphur dioxide, a copper enolate was given, identical with that prepared from authentic ethyl *trans*-β-carbethoxyacrylylmalonate. The inversion of the *cis*-ester product (VII*b*) to the established *trans*-form (VII*a*) thus left the chemical constitution of the former in no doubt whatever, whilst the steric configuration was proved by the cleavage reaction.

Now in their work on the muconic acids, Elvidge, Linstead, Sims, and Orkin (*J.*, 1950, 2235) assumed that, in ring-opening of the lactone (II) with sodium alkoxide to give a doubly-



(II.) (XXV.)

unsaturated acyclic product (XXV), the *cis*-configuration about the double bond • in the lactone was preserved in the acyclic product. This assumption was confirmed by a self-consistent series of chemical transformations, but no direct correlation with compounds of established steric configuration was possible.

In the present work we have been able to relate the acyclic products obtained by ring-opening of the lactone (IV) directly to maleic and fumaric acids. The finding that only the reaction with sodium alkoxide leads to a *cis*-product, uncontaminated with any detectable amount of *trans*-material, is of particular interest and confirms the validity of the argument in our earlier paper.

Experimental.

Ethyl trans-*β-Carbomethoxyacrylylmalonate* (XI).—According to the directions of Erlenmeyer (*Helv. Chim. Acta*, 1937, **20**, 1008) methyl fumarate (2 × 72 g.) was hydrolysed to methyl hydrogen fumarate (75 g., 58%; m. p. 141°, from water). This with an excess of thionyl chloride at 100° afforded *trans*-β-carbomethoxyacrylyl chloride (65 g.; b. p. 55—60°/6 mm.), which was treated in ether with ethyl magnesiomalonate (from 72 g. of ethyl malonate) following the method of Riegel and Lilienfeld (*J. Amer. Chem. Soc.*, 1945, **67**, 1273). The mixture was stirred and heated under reflux for 2 hours, then cooled and cautiously treated with 2N-sulphuric acid. The aqueous layer was extracted with ether, and the combined organic solutions were washed successively with dilute sulphuric acid, water, a small volume of aqueous sodium hydrogen carbonate, and water. After being dried ($MgSO_4$) and concentrated, finally under reduced pressure, a brown oily residue was obtained which deposited solid (S) (27 g.; m. p. 45—80°). The oil was decanted and distilled under reduced pressure to give: (i) forerun, b. p. 50—120°/0·15 mm. (12·5 g.) (largely ethyl malonate); (ii) b. p. 150—160°/1 mm., m. p. 43—110° (26·9 g.); (iii) b. p. 160—167°/1·5 mm., m. p. 47—48° (32·5 g.). The last fraction contained mainly *ethyl* trans-*β-carbomethoxyacrylylmalonate*, which crystallised from light petroleum (b. p. 40—60°) as prisms, m. p. 54—54·5° (Found: C, 52·8; H, 6·0. $C_{12}H_{14}O_7$ requires C, 52·9; H, 5·9%). Its solution in aqueous sodium hydrogen carbonate is yellow, and it gives a blood-red colour with ferric chloride in aqueous alcohol. Fraction (ii) contained methyl hydrogen fumarate (1·46 g.; m. p. 130—140°), separated by filtration at 50°.

trans-1 : 1 : 6 : 6-*Tetracarbethoxyhex*-3-*ene*-2 : 5-*dione* (VIII).—The solid S (above) crystallised from methanol to give the *tetraethyl* ester (VIII) as cream-coloured needles, m. p. 117° (Found: C, 54·0; H, 6·0. $C_{18}H_{24}O_{10}$ requires C, 54·0; H, 6·0%), which gave a red ferric chloride colour. From the mother-liquors, methyl fumarate was isolated, m. p. 97—100° undepressed in admixture with an authentic specimen.

Fumaryl chloride (34·8 g.; b. p. 56—59°/18—19 mm.; prepared in 81% yield by heating fumaric acid with 2 mols. of phosphorus pentachloride on the steam-bath for 1 hour) in dry ether (200 c.c.) was added during 2 hours to a stirred solution of ethyl magnesiomalonate (from 80 g. of ethyl malonate) in dry ether (300 c.c.), and the mixture heated under reflux for 3 hours longer. Next day, the mixture was decomposed with cold 2N-sulphuric acid (300 c.c.), whereupon the ester (VIII) crystallised (58 g., 64%; m. p. 106—110°). When the ester (1 g.) was heated in chloroform with phenylhydrazine (0·5 c.c., 2 mols.) under reflux for 1 hour, trans-1 : 2-*di*-(5-*keto*-1-*phenyl*-4-*phenylhydrazido*-3-*pyrazolinyl*)*ethylene* separated and was obtained from pyridine–light petroleum (b. p. 100—120°) as a yellow micro-crystalline powder, m. p. 291—292° (decomp.) (Found: N, 18·5. $C_{24}H_{18}O_4N_8$ requires N, 18·3%).

The ester (VIII) (8 g.) in propionic acid (24 c.c., 16 mols.) containing toluene-*p*-sulphonic acid (0·32 g.) was boiled under reflux for 13 hours. The solution was cooled, made alkaline with aqueous sodium carbonate, and extracted with ether, and the organic layer was dried ($MgSO_4$) and evaporated. Treatment of the residue with methanolic 2 : 4-dinitrophenylhydrazine yielded the derivative of ethyl β-acetyl-

acrylate, which crystallised from methanol as plates, m. p. 147° (lit., m. p. 150°) (Found: C, 48·5; H, 4·65; N, 16·9. Calc. for $C_{12}H_{14}O_8N_4$: C, 48·3; H, 4·7; N, 17·3%).

Reactions of Ethyl trans-*β-Carbomethoxyacrylylmalonate.*—(a) *Condensation with phenylhydrazine.* On keeping the tri-ester (1·37 g.) in alcohol with phenylhydrazine (0·5 c.c.) in 50% aqueous acetic acid (4 c.c.) for 2 days, colourless needles of *methyl 4-carbethoxy-5-keto-1-phenylpyrazoline-3-β-trans-acrylate* separated, which after three crystallisations from carbon tetrachloride–light petroleum (b. p. 60—80°) had m. p. 147° (Found: N, 8·9. $C_{16}H_{14}O_5N_2$ requires N, 8·9%).

(b) *Fission with aqueous potassium hydroxide.* A solution of the tri-ester (1 g.) in N-potassium hydroxide (15 c.c.) was kept at room temperature overnight, and then acidified. Solid separated (0·18 g.; m. p. 94°), and was identified as ethyl *trans-β*-carboxyacrylylmalonate (XIII) (see below). The filtrate was extracted continuously with ether overnight, and the extract dried ($MgSO_4$) and evaporated to give a residue (0·6 g.), which was extracted with acetone. Fumaric acid (0·1 g.; m. p. 290° with sublimation) remained undissolved. The filtrate was evaporated to dryness, the residue extracted with benzene, and the extract filtered and treated with light petroleum (b. p. 60—80°). Malonic acid separated (0·14 g.; m. p. 105—120°), which after crystallisation from ethyl acetate had m. p. 127—129° (decomp.), and m. p. 130° when mixed with an authentic specimen.

(c) *Bromination.* A solution of the tri-ester (15·8 g.) in chloroform was kept with bromine (9·3 g., 1 mol.) at 0° overnight, then evaporated, finally under reduced pressure. *Ethyl β-carbomethoxy*(erythro)-*αβ-dibromopropionylmalonate* (XII) (11·7 g.) crystallised from light petroleum (b. p. 40—60°) in rhombs, m. p. 67—68° (Found: C, 33·3; H, 3·75. $C_{12}H_{16}O_7Br_2$ requires C, 33·35; H, 3·7%). It was unchanged by stirring with concentrated hydrobromic acid (150 c.c.; *d* 1·5) for 6 days: no αβ-dibromo-β′-ketoadipic acid was found in the filtrate.

(d) *Methanolysis.* The tri-ester (5 g.) was treated overnight with saturated methanolic hydrogen chloride (50 c.c.) containing concentrated aqueous hydrochloric acid (5 c.c.). On evaporation under reduced pressure, a mixture (3·65 g.) of a solid, m. p. 90—100°, with an oil was obtained. The solid, washed with a small quantity of methanol, and crystallised from light petroleum (b. p. 60—80°), was identified (mixed m. p.) as methyl dihydro-β-ketomuconate (below).

(e) *Hydrolysis with methanolic lithium hydroxide.* The tri-ester (2·7 g.) was allowed to react overnight with methanolic 0·34N-lithium hydroxide (90 c.c., 3 equivs.). The solvent was removed under reduced pressure, the residue dissolved in water, and the solution acidified. Ethyl β-carboxyacrylylmalonate (0·3 g.) separated, m. p. 97—98°, and m. p. 100—101° when mixed with an authentic specimen (see below). On concentration of the filtrate under reduced pressure fumaric acid (0·3 g.), m. p. 280° (with sublimation), was obtained.

Attempted Preparation of cis-*β-Carbethoxyacrylyl Chloride.*—A solution of maleic anhydride (100 g.) in ethanol (60 c.c.) was heated on the steam-bath for 1 hour, cooled, treated with thionyl chloride (110 c.c.) and then heated under reflux for 1 hour longer. Distillation under reduced pressure (20 mm.) through a Dufton column (8″) afforded a liquid of steadily increasing b. p. and falling refractive index (n_D^{21}), collected in the following arbitrary fractions: (i) 86—88°, 1·4643 (56 g.); (ii) 88—94°, 1·4620; (iii) 94—100°, 1·4575; (iv) 100—105°, 1·4535 (Found: C, 38·85; H, 4·35. Calc. for $C_6H_7O_3Cl$: C, 44·3; H, 4·3. Calc. for $C_6H_6O_3Cl_2$: C, 36·2; H, 4·0%) [(ii) + (iii) + (iv) = 27·5 g.]. 1-G. portions of fractions (i) and (iv) were added dropwise, with stirring, to separate solutions of *p*-aminobenzenesulphonamide (2·2 g.) in dry dioxan (15 c.c.). After 5 minutes, each mixture was diluted with water to 250 c.c. and cooled in ice. Recrystallisation of the precipitates from *n*-butanol yielded, respectively, needles (0·95 g.) (negative Beilstein test), m. p. 219°, of fumaric half-ethyl ester half-sulphanilamide (Bergmann and Schapiro, *loc. cit.*, give m. p. 219°), and plates (0·55 g.) (positive Beilstein test), m. p. 190—195° (depressed to 175—178° by the preceding amide), presumably of mixed stereoisomeric chlorosuccinyl half-ethyl ester half-sulphanilamides (Found: C, 43·6; H, 4·7; N, 8·8. Calc. for $C_{12}H_{15}O_5N_2ClS$: C, 43·1; H, 4·5; N, 8·4%).

Ethyl Hydrogen Fumarate.—A *well-mixed* solution of maleic anhydride (100 g.) in hot ethanol (60 c.c.) was treated with thionyl chloride (1 c.c.) and heated on the steam-bath for 5—10 minutes. Carbon tetrachloride (100 c.c.) was added cautiously, and the hot mixture filtered (with gentle suction through 2 papers on a warm funnel, ~10 cm. diam., to obviate clogging). The fumaric acid (7—12 g. in different runs), m. p. 286° (with sublimation), was washed with boiling carbon tetrachloride (15 c.c.), and the combined filtrate cooled thoroughly in ice. The paste was transferred to a filter, drained, washed with cold carbon tetrachloride (2 × 20 c.c.), and dried: yield, 100—95 g., plates, m. p. 67—68° undepressed by authentic material from half-hydrolysis of ethyl fumarate. When the heating (following the thionyl chloride addition) was prolonged to 15 minutes, the yield fell to 88 g. and more fumaric acid (16 g.) was formed.

trans-*β-Carbethoxyacrylyl Chloride.*—Ethyl hydrogen fumarate (100 g.) and thionyl chloride (100 c.c.) were heated on the steam-bath under reflux for 1·5 hours, and the product fractionated under reduced pressure to give fumaric half-ester chloride (92 g., 82%), b. p. 74—75°/10 mm., 86°/20 mm., n_D^{22} 1·4610.

Methyl Hydrogen Fumarate.—A warm *well-mixed* solution of maleic anhydride (100 g.) in methanol (50 c.c.) was treated with thionyl chloride (1 c.c.) and heated on the steam-bath for 10 minutes. On cooling, the mixture set to a solid. This was stirred vigorously with excess of aqueous sodium hydrogen carbonate, and the insoluble material collected, washed with water, and recrystallised from methanol–benzene to give methyl fumarate (51 g.), m. p. 98—100°. The aqueous filtrate was concentrated under reduced pressure to ~150 c.c. (to remove any methanol), and then cooled in ice and acidified to thymol-blue with concentrated hydrochloric acid. The precipitate (m. p. >200° with softening at ~135°) was extracted with boiling chloroform: insoluble fumaric acid (12·5 g.) remained. On concentration and cooling, the extract afforded pure methyl hydrogen fumarate (21·5 g., 16%), m. p. 141°.

trans-*β-Carbomethoxyacrylyl Chloride*.—Methyl hydrogen fumarate (21·5 g.) and excess of thionyl chloride (70 c.c.) were heated on the steam-bath under reflux for 1 hour, and the product fractionated to yield the half-chloride (20 g., 81%), b. p. 76°/20 mm., n_D^{20} 1·4710.

Methyl trans-*β-Carbomethoxyacrylylmalonate* (VII; R = R′ = Me).—Methyl malonate (20 g.) in methanol (9 c.c.) was added to a mixture of magnesium powder (3·3 g.), dry methanol (3·3 c.c.), and carbon tetrachloride (0·2 c.c.). When the initially vigorous reaction had subsided, methanol (20 c.c.) and dry ether (100 c.c.) were added, and the mixture was heated under reflux overnight. By evaporation, and repeated distillation to dryness with dry benzene (3 × 100 c.c.), finally under reduced pressure, the excess of methanol was removed. The magnesium complex, dissolved in benzene (100 c.c.), was then treated dropwise with *trans*-*β*-carbomethoxyacrylyl chloride (20 g.) in benzene (30 c.c.), and the stirred mixture heated under reflux for 3 hours. Next day, the mixture was shaken mechanically with 2N-sulphuric acid, the aqueous layer extracted with ether, and the combined organic solution washed with a small volume of aqueous sodium hydrogen carbonate and water, and dried ($MgSO_4$). The solvent was distilled, and the solid residue (28·3 g., 87%) purified by dissolution in dilute sodium hydroxide and precipitation with hydrochloric acid. From light petroleum (b. p. 40—60°) *methyl* trans-*β-carbomethoxyacrylylmalonate* formed colourless needles, m. p. 89° (Found: C, 49·1; H, 5·1. $C_{10}H_{12}O_7$ requires C, 49·2; H, 4·9%). The ester gives a red colour with ferric chloride in aqueous alcohol.

Ethyl trans-*β-Carbethoxyacrylylmalonate* (VIIa).—*trans*-*β*-Carbethoxyacrylyl chloride (112·4 g.) and ethyl magnesiomalonate [from ethyl malonate (120 g.) and magnesium turnings (16·6 g.)] were allowed to react in ether, and the complex decomposed in the usual manner [as for (XI)] to yield *ethyl* trans-*β-carbethoxyacrylylmalonate* (149 g., 75%), b. p. 144°/0·5 mm., 110—111°/2 × 10^{-2} mm., n_D^{20} 1·4960 (Found: C, 54·2; H, 6·2. $C_{13}H_{18}O_7$ requires C, 54·5; H, 6·3%). It gives a red colour with ferric chloride.

Treatment of the ester (1·43 g.) in ethanol with cupric acetate (0·5 g.) in a minimum of water gave an oil which solidified on scratching (1·27 g.; m. p. 153—154°); a second crop (0·12 g.; m. p. 156—158°) separated from the filtrate on addition of water. From aqueous ethanol the *copper* enolate of the *trans*-keto-ester (VIIa) formed shining green plates, m. p. 159—159·5° [Found: C, 49·2; H, 5·6. $(C_{13}H_{17}O_7)_2Cu$ requires C, 49·2; H, 5·4%].

Ethyl trans-*β-Carboxyacrylylmalonate* (XIII).—(a) Ethyl *trans*-*β*-carbomethoxyacrylylmalonate (XI) (1 g.) was dissolved in potassium hydroxide (1·5 g.) in methanol (5 c.c.). After 2 days, dilute hydrochloric acid was added, and the precipitated *ethyl* trans-*β-carboxyacrylylmalonate* (0·46 g., 54%) crystallised from benzene–light petroleum (b. p. 60—80°) in white needles, m. p. 107° (Found: C, 51·2; H, 5·6. $C_{11}H_{14}O_7$ requires C, 51·2; H, 5·5%). It gives a red colour with ferric chloride.

(b) Ethyl *trans*-*β*-carbethoxyacrylylmalonate (VIIa) (40 g.) in ethanol (1 vol.) was added to a solution of potassium hydroxide (32 g.) in ethanol (200 c.c.) and kept overnight. The potassium salt was collected, washed with alcohol and ether, and dissolved in a minimum of water, and the ice-cooled solution acidified with concentrated hydrochloric acid. The precipitated ethyl *trans*-*β*-carboxyacrylylmalonate (34·1 g., 95%; m. p. 102°) was sufficiently pure for lactonisation.

trans-*Dihydro-β-ketomuconic* (trans-3-*Ketobut*-1-*ene*-1 : 4-*dicarboxylic*) *Acid* (XV).—(a) A solution of ethyl *trans*-*β*-carbomethoxyacrylylmalonate (XI) (5 g.) in acetic acid (20 c.c.) and concentrated hydrochloric acid (10 c.c.) was saturated with gaseous hydrogen chloride, and kept at room temperature for 2 days. A white solid (1 g.) separated, which from acetone–light petroleum (b. p. 40—60°) gave trans-*dihydro-β-ketomuconic acid* as a microcrystalline powder, m. p. 164° (decomp.) (Found: C, 45·7; H, 3·8. $C_6H_4O_5$ requires C, 45·6; H, 3·8%). The acid gives a deep purple colour with ferric chloride in aqueous alcohol.

In another experiment, the ester (XI) (32 g.) was dissolved in formic acid, concentrated hydrochloric acid (50 c.c.) was added, and the suspension redissolved by addition of more formic acid. After treatment with gaseous hydrogen chloride, the solution was kept at 30° for 4 days. The acid which separated (8·7 g.) had an indefinite m. p.: it was twice extracted with boiling acetone, and the combined filtrate treated progressively with light petroleum (b. p. 40—60°) to yield fumaric acid, m. p. 285° (with sublimation), and two crops of nearly pure dihydro-*β*-ketomuconic acid, m. p. 152—155° (decomp.) and 165—167° (decomp.).

(b) A solution of methyl *trans*-*β*-carbomethoxyacrylylmalonate (VII; R = R′ = Me) (5 g.) in acetic acid (100 c.c.) and concentrated hydrochloric acid (100 c.c.) was kept at room temperature for 6 days, then evaporated to dryness under reduced pressure, and the residue extracted with acetone. Dihydro-*β*-ketomuconic acid (0·62 g.), m. p. 167° (decomp.) (contaminated with traces of fumaric acid), remained undissolved.

Reactions of Dihydro-β-ketomuconic Acid.—(a) *Decarboxylation*. The acid (0·5 g.) was boiled in water for 15 minutes, and the solution evaporated to dryness under reduced pressure. Extraction of the residue (0·34 g.), m. p. 112—117°, with benzene left fumaric acid (0·03 g.), m. p. and mixed m. p. 290° (with sublimation), and from the filtrate, *β*-acetylacrylic acid (0·14 g.) crystallised with m. p. and mixed m. p. 118—120° [authentic material, prepared from lævulic acid (Wolff, *Annalen*, 1891, **264**, 229), had m. p. 122—123°].

(b) *Hydrogenation*. The acid (XV) (1 g.) in alcohol (50 c.c.) was shaken in hydrogen in the presence of Adams's catalyst (100 mg.). Uptake (235 c.c. at 25°/765 mm. Calc. for 2 mols: 308 c.c.) ceased after 2 hours. The filtered solution was evaporated under reduced pressure to leave an oily residue (0·7 g.), from which crude *β*-ketoadipic acid crystallised (0·21 g., 20%), m. p. 94° (decomp.): it was separated by washing with ether–hexane, and characterised as lævulic acid semicarbazone, m. p. and mixed m. p. 184° (decomp.).

After a solution of *β*-ketoadipic acid (1·6 g.) in ethanol (20 c.c.), containing Adams's catalyst (100 mg.), had been shaken with hydrogen under similar conditions for 19 hours (no uptake), an oily residue was eventually obtained. This afforded lævulic acid 2 : 4-dinitrophenylhydrazone in 73% yield, m. p. 201—202°, and 203° when mixed with an authentic specimen.

(c) *Esterification.* The acid (XV) (0·5 g.) in methanol (100 c.c.) was treated with ethereal diazomethane, the solution evaporated under reduced pressure, and the residual solid extracted with ether. The ether was filtered and evaporated, and the residue sublimed at 100°/20 mm. and recrystallised from *cyclo*hexane to give *methyl* trans-*dihydro-β-ketomuconate* (XIV) as shining needles, m. p. 95·5—98° (Found: C, 51·4; H, 5·4. $C_8H_{10}O_5$ requires C, 51·6; H, 5·4%). The ester gives a red colour with ferric chloride in aqueous alcohol.

(d) *Bromination.* To the acid (XV) (1·6 g.) suspended in acetic acid (50 c.c.), bromine (1·6 g., 1 mol.) in acetic acid was added slowly with stirring. Unchanged material (0·2 g.) was filtered off, the solution evaporated to dryness under reduced pressure, and the residue (1·25 g., 45%) washed with chloroform and light petroleum. From ethyl acetate–carbon tetrachloride (erythro)-*αβ-dibromo-β'-ketoadipic acid* (XVIII) crystallised as needles, m. p. 148—149° (decomp.) (Found: Br, 50·3. $C_6H_6O_5Br_2$ requires Br, 50·3%). The acid gives a deep purple with ferric chloride.

α-Bromo-γ-carboxymethylenebutenolide (XX).—The preceding acid (1·5 g.) was kept with acetyl chloride (20 c.c.) for 3 days at room temperature and the solution then evaporated under reduced pressure, finally in a desiccator. The *lactone* crystallised from chloroform and ethyl acetate–light petroleum (b. p. 60—80°) as minute prisms, m. p. 182—183° (decomp.) (Found: C, 32·9; H, 1·8. $C_6H_3O_4Br$ requires C, 32·9; H, 1·4%). It does not give a ferric chloride colour.

Lactonisation Experiments with Dihydro-β-ketomuconic Acid.—(a) A suspension of the acid (1 g.) in acetyl chloride (25 c.c.) was heated under reflux for 24 hours and filtered, and the filtrate evaporated under reduced pressure to afford a brown syrup. This gave a red ferric chloride colour and on exposure to the air slowly solidified. Crystallisation from acetone–light petroleum (b. p. 40—60°) gave starting material (0·29 g.), m. p. and mixed m. p. 154° (decomp.).

(b) *γ-Carboxymethylenebutenolide* (III; R = H). The acid (XV) (2 g.), acetic anhydride (20 c.c.), and acetic acid (20 c.c.) were heated together on the steam-bath for 2 hours, whilst hydrogen bromide was passed through. The solution was evaporated under reduced pressure, and the residue (1·1 g.) taken up in acetone, and treated with charcoal. The filtrate was concentrated, filtered from sparingly-soluble matter, and evaporated under reduced pressure, the residue taken up in ethylene dichloride, and the solution again clarified and then cooled in ice. *γ-Carboxymethylenebutenolide* crystallised from ethylene dichloride as needles (75 mg.), m. p. 156° (Found: C, 51·7; H, 3·1. $C_6H_4O_4$ requires C, 51·4; H, 2·9%). It does not give a colour with ferric chloride. Treatment in ether with ethereal diazoethane (Adamson and Kenner, *J.*, 1937, 1551) afforded an ester identified by mixed m. p. with that next described.

Pyrolysis of Ethyl trans-*β-Carbethoxyacrylylmalonate.*—(a) The ester (VII*a*) (20·8 g.) and naphthalene-β-sulphonic acid (1 g.) were heated to 190° during 30 minutes. Vigorous evolution of gas took place at 140—160°. The cooled reaction product was taken up in ether, washed with 5% sodium hydrogen carbonate (35 c.c.) and water, dried ($MgSO_4$), and evaporated: distillation under reduced pressure failed to afford any material of constant b. p., but from a fraction of b. p. 100—118°/0·5—1 mm., a neutral solid crystallised on standing. From light petroleum (b. p. 60—80°), *γ-carbethoxymethylenebutenolide* (III; R = Et) (150 mg.) formed prisms, m. p. 77·5—78·5° (Found: C, 57·0; H, 5·0. $C_8H_8O_4$ requires C, 57·1; H, 4·8%). It does not give a colour with ferric chloride.

(b) The triester (30 g.) and naphthalene-β-sulphonic acid (3 g.) were heated rapidly (5—10 minutes) to 250° and kept at that temperature for 20 minutes. The product was worked up as previously, and the following fractions were collected at 0·05 mm.: (i) b. p. 50—100°; (ii) 100—125°; (iii) 125—170°. At 0°, fraction (i) deposited a crystalline solid (82 mg.), m. p. 77—78·5° alone and in admixture with γ-carbethoxymethylenebutenolide, whilst (ii) and (iii) solidified partially: the solids had m. p.s 41—55° (0·6 g.) and 58—60° (1·76 g.), respectively. After single crystallisations from ether–light petroleum (b. p. 40—60°), these two solids had m. p.s 47—58° and 59—61°: the latter was not depressed by γ-dicarbethoxymethylenebutenolide (below).

γ-Dicarbethoxymethylenebutenolide (IV).—Ethyl β-carboxyacrylylmalonate (XIII) (7·5 g.) was heated in acetic anhydride (80 c.c.) on the steam-bath for 6 hours whilst dry hydrogen bromide was passed through. The solution was evaporated to dryness under reduced pressure, and the residue distilled at 100°/10^{-4} mm. *γ-Dicarbethoxymethylenebutenolide* (6·0 g., 73%) was obtained as a pale yellow solid which crystallised from ether–light petroleum (b. p. 40—60°) as colourless prisms, m. p. 62° [Found: C, 54·8; H, 5·1%; *M* (Rast), 215. $C_{11}H_{12}O_6$ requires C, 55·0; H, 5·0%; *M*, 240]. The lactone crystallises with great ease and is readily soluble in most organic solvents.

Attempted Decarbethoxylation of (IV).—(a) The lactone (10 g.) and naphthalene-β-sulphonic acid (1 g.) were heated to 250° (*ca.* 30 minutes): slight evolution of gas occurred at 150—160°. The dark oil was cooled, taken up in ether, and filtered, and the solution washed with aqueous sodium hydrogen carbonate and water. After being dried ($MgSO_4$), the ether was evaporated, and the residue distilled at 100°/10^{-4} mm. The distillate (4·8 g.) slowly crystallised and then had m. p. 51—56° alone and in admixture with the starting material.

(b) The lactone (7·2 g.), propionic acid (40 c.c.; redistilled), propionic anhydride (2 c.c.), and toluene-*p*-sulphonic acid (0·4 g.) were heated together in a flask surmounted by a fractionating column and a total-reflux, variable-take-off head. During 11 hours, 2 c.c. of distillate were collected, which had an odour of ethyl propionate but were completely soluble in alkali. The distilland was concentrated under reduced pressure and taken up in ether. The solution was washed with sodium hydrogen carbonate and water, dried ($MgSO_4$), and evaporated, and the residue distilled at 100°/10^{-4} mm., to yield a solid (5·16 g.), m. p. 45—50°, which after recrystallisation from ether–light petroleum had m. p. 59—61° alone and in admixture with the starting material.

Properties of the Lactone (IV).—(a) *Colour reactions.* The lactone did not give a colour immediately with ferric chloride in aqueous alcohol: on standing overnight, or on boiling, a red colour developed.

The Légal test was negative. Ammoniacal silver nitrate and dichlorophenol-indophenol were not reduced (cf. Kuehl, Linstead, and Orkin, *J.*, 1950, 2213).

(b) *Stability to water.* A solution of the lactone (0·5 g.) in dioxan (4·5 c.c.) and water (3·5 c.c.) was kept at room temperature for 22 hours, then evaporated to dryness under reduced pressure. The oily residue gave a very faint red colour with ferric chloride, and on seeding with the starting material it solidified (0·42 g., 84%), m. p. and mixed m. p. 48—51°.

(c) *Fission with aqueous alkali.* The lactone (2·4 g., 0·01 mol.) in dioxan (50 c.c.) was treated with 0·1N-potassium hydroxide (100 c.c., 1 equiv.), and after 3 days the solution was concentrated under reduced pressure at <37°, acidified with 2N-sulphuric acid (5 c.c.), and extracted with ether for 6 hours. By evaporation of the extract, maleic acid (1·44 g.) was obtained, which after being washed with cold chloroform and crystallised from ethyl acetate, had m. p. and mixed m. p. 135—136°. Vacuum sublimation at 160—170° gave maleic anhydride, m. p. 51—53° not depressed by an authentic specimen. The chloroform washings from the maleic acid were evaporated to dryness, and the residue kept with ammonia solution (*d* 0·88) for several days. Aqueous barium hydroxide was added, barium maleate removed, the filtrate evaporated to dryness under reduced pressure, and the residue twice extracted with boiling dioxan. Evaporation of the filtered extract under reduced pressure afforded malonamide, m. p. 163—164° (decomp.) undepressed by authentic material.

(d) *Hydrogenation.* (i) Reduction of the lactone (0·6 g.) in ethanol (5 c.c.) with hydrogen (at room temperature and pressure) and Adams's catalyst (50 mg.) was essentially complete in 2 hours (Hydrogen uptake, after 5 hours: 149 c.c. Calc. for 3 mols.: 165 c.c.). The filtered solution was concentrated under reduced pressure, and the oily residue heated under reflux with potassium hydroxide (0·75 g.) in water (3·5 c.c.) for 1·5 hours. Acidification with hydrochloric acid, evaporation to dryness under reduced pressure, and extraction with ether gave crude α-carboxyadipic acid (0·33 g.; m. p. 95—105°), separated by crystallisation from ethyl acetate–benzene into fractions of m. p. 132—133° and 110—115° (Ruggli and Maeder, *Helv. Chim. Acta*, 1943, **26**, 1476, give m. p. 139° for α-carboxyadipic acid). Each fraction on pyrolysis yielded adipic acid, m. p. 146° (from water), and m. p. 148° when mixed with authentic material.

(ii) The lactone (0·84 g.) in purified ethyl acetate was 50% hydrogenated in the presence of Adams's catalyst (50 mg.). The allowed uptake of hydrogen (122 c.c. at 24°/762 mm.) (Calc. for 3 mols.: 255 c.c.) took 1 hour. The dark solution was filtered and evaporated under reduced pressure, and the oily residue (0·76 g.) in ether was separated by extraction with aqueous sodium hydrogen carbonate into an acid fraction (0·31 g.) and a neutral oil (0·24 g.). The latter crystallised on cooling and after distillation at 170—190°/0·05 mm. had m. p. 47°, and m. p. 52—53° when mixed with the starting material. The acid fraction was boiled under reflux with concentrated hydrochloric acid (10 c.c.) for 3 hours, and the solution treated with charcoal and evaporated to dryness under reduced pressure. The residue crystallised from ethyl acetate–light petroleum (b. p. 60—80°) with m. p. 143—145°: a mixture with adipic acid had m. p. 147—149°.

(e) *Reaction with ethanol.* (i) A solution of the lactone in ethanol gave, on spontaneous evaporation, only unchanged material, m. p. and mixed m. p. 60°. (ii) The lactone (0·5 g.) in dry ethanol (10 c.c.) was heated under reflux for 2·5 hours, and next day the solution was evaporated to dryness under reduced pressure. The residue, which gave a faint red with ferric chloride, soon set to a solid (0·27 g., 54%), m. p. 53—55° (softened at 42°) alone and in admixture with the starting material. (iii) A solution of the lactone (0·5 g.) in dry ethanol (10 c.c.) containing a trace of hydrogen chloride was boiled under reflux for 2·5 hours and evaporated under reduced pressure. Treatment of the mobile oily residue in alcohol with aqueous cupric acetate afforded the copper enolate of ethyl *trans*-β-carbethoxyacrylylmalonate, m. p. 141—143°, and m. p. 151° when mixed with an authentic specimen.

(f) *Reaction with sodium ethoxide. Formation of ethyl* cis-β-*carbethoxyacrylylmalonate* (VII*b*). The lactone (1·2 g., 0·005 mol.) in dry ethanol (20 c.c.) was kept for 30 minutes with ethanolic sodium ethoxide (5 c.c.; N.). The solvent was evaporated, the residue taken up in water, and the solution acidified to thymol-blue with dilute sulphuric acid and extracted with ether. Evaporation of the extract afforded a mobile oil (1·2 g.) which gave a bright red colour with ferric chloride: portions were treated separately as follows:

(i) On addition of cupric acetate (0·15 g.) in water (6 c.c.) to the oil (0·16 g.) in ethanol (2 c.c.) and cooling in ice and stirring with a glass rod, a green solid separated (0·12 g.), m. p. 49—55°. From aqueous ethanol, the *copper* enolate (*form A*) of ethyl *cis*-β-carbethoxyacrylylmalonate crystallised as green solvated needles, m. p. 54—55° (Loss in weight on drying at 20 mm. over silica gel: 5·6%) [Found, on dried material: C, 48·0; H, 5·5. $(C_{12}H_{17}O_7)_2Cu,H_2O$ requires C, 47·9; H, 5·6%]. During the recrystallisation of form A, green needles, m. p. 101—102°, of *form B* were obtained (Loss in weight on drying as above: 4·35%) (Found, on dried material: C, 48·0; H, 5·45%).

A mixture of A and B softened at ~64° and had m. p. 101—101·5°. Mixtures of the copper enolate of ethyl *trans*-β-carbethoxyacrylylmalonate (plates, m. p. 159°) with A and B melted progressively from 51° and 94°, respectively. Form A was unchanged by crystallisation from ethanol–water and seeding with B. Form B was converted into A by similar crystallisation and seeding with A. In a vacuum desiccator over calcium chloride, form A fell to a dark glass which on exposure to the air resolidified (becoming pale green) and then had m. p. 100—101° alone and in admixture with B: on further drying, the enolate became dark and glassy once more. The water of constitution was not removed at 10^{-4} mm. over phosphoric oxide (Found: C, 47·7; H, 5·6%).

(ii) A solution of the oil in ethanol containing traces of hydrogen chloride and sulphur dioxide was kept at room temperature for 3 days, then evaporated under reduced pressure and again after addition of fresh ethanol. The residue in ethanol was treated with aqueous cupric acetate to yield a copper enolate, m. p. 149·5—151·5°, which, after one crystallisation from ethanol–water, had m. p. 154—155°, and m. p. 158° when mixed with the copper enolate of ethyl *trans*-β-carbethoxyacrylylmalonate.

(iii) The oil (0·54 g.) was dissolved in aqueous sodium hydroxide (10 c.c.; 1·04N.). Next day, the solution was acidified to thymol-blue with dilute sulphuric acid and extracted with ether for 7 hours. The ether was evaporated, and the residue taken up in ether (1 c.c.), cooled, and scratched. The solid which separated was washed with ether–hexane (3 : 2) and then had m. p. 136—137°, and m. p. 137° in admixture with maleic acid (m. p. 137°); the yield was 17 mg. A mixture with malonic acid had m. p. 108—111° (after softening at 75°). It was found that a solution of maleic acid in ethyl acetate when treated with traces of hydrogen chloride and sulphur dioxide deposited a nearly equal weight of fumaric acid during 24 hours. The preceding filtrate and washings were accordingly evaporated, and the residue in ethyl acetate treated similarly: sparingly soluble fumaric acid separated (60 mg.), recognised by m. p. and mixed m. p.

(g) *Reaction with aniline.* The lactone (0·9 g.) in dioxan was kept with aniline (0·35 g., 1 mol.) overnight. Removal of the solvent under reduced pressure afforded an oil which solidified to a yellow mass (0·77 g.; m. p. 111—112°). This was washed with ether and crystallised from benzene and aqueous ethanol to yield *ethyl* trans-*β-anilidoacrylylmalonate* (XXIV) as beautiful pale yellow needles, m. p. 114—114·5°, identical with the material synthesised below (Found: C, 61·3; H, 5·9; N, 4·4. $C_{17}H_{19}O_6N$ requires C, 61·25; H, 5·7; N, 4·2%). After treatment at room temperature for several days in ethanol containing traces of hydrogen chloride and sulphur dioxide, the anilide was recovered, m. p. 106—109° not depressed by the starting material.

Synthesis of Ethyl trans-*β-Anilidoacrylylmalonate.*—(a) Fumaric half-anilide half-chloride (2 g.; m. p. 119—120°) (Anschütz, *Annalen*, 1890, **259**, 137) in benzene (100 c.c.) was heated with a benzene solution (50 c.c.) of ethyl magnesiomalonate (from 3·2 c.c. of malonic ester and 0·5 g. of magnesium) for 6 hours on the steam-bath. The cooled mixture was shaken with 2N-sulphuric acid (30 c.c.), and the benzene layer separated, washed with water, filtered, and evaporated. The residue crystallised on treatment with ether and had m. p. 110—111°, and m. p. 113—114° in admixture with the anilide obtained from the lactone.

(b) Ethyl *trans-β*-carboxyacrylylmalonate (1·3 g.) in dry benzene containing pyridine (1 drop) was treated with oxalyl chloride (0·5 c.c.) at 0°. The solution was warmed to room temperature and after 1·5 hours was heated at 40° for a further 1·5 hours, and then evaporated under reduced pressure. Dry benzene was added and evaporated again, and to the residual oil in dry ether aniline (0·9 c.c., 2 mols.) in ether was added slowly at 0° with shaking. The mixture was washed successively with water, dilute acid, sodium hydrogen carbonate, and water, and the ethereal solution dried ($MgSO_4$) and evaporated. The anilide (1·14 g.; m. p. 110°) crystallised from benzene–light petroleum (b. p. 60—80°) with m. p. 111—112° undepressed by the product from the lactone (IV) and aniline.

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346. *A Method for Preparing Secondary Amines and Schiff's Bases from Phenols and Hexamine.*

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Phenols heated with hexamine and boric acid in 2-ethoxyethanol form secondary amines of the type OH·X·CH_2·NH·CH_2·X·OH (H·X·OH = the phenol). Dehydrogenation of these amines by heating them with hexamine in acetic acid produces Schiff's bases of the type OH·X·CH:N·CH_2·X·OH which can be hydrolysed to phenolic aldehydes. These reactions are regarded as explaining the mechanism of the general method for preparing *o*-hydroxy-aldehydes described by Duff (*J.*, 1941, 547). New secondary amines and Schiff's bases from eleven phenolic compounds are described.

A GENERAL method for preparing *o*-hydroxy-aldehydes from phenols and hexamine has been described by one of the authors (Duff, *J.*, 1941, 547). The reaction conditions in the anhydrous medium, glyceroboric acid, prevented identification of the intermediate compounds which yielded aldehydes on hydrolysis. It was recorded that the stages of the reaction might be

$$3H{\cdot}X{\cdot}OH + C_6H_{12}N_4 \longrightarrow NH_3 + 3OH{\cdot}X{\cdot}CH_2{\cdot}N{:}CH_2$$

followed by isomerisation and hydrolysis:

$$OH{\cdot}X{\cdot}CH_2{\cdot}N{:}CH_2 \longrightarrow OH{\cdot}X{\cdot}CH{:}N{\cdot}CH_3 \xrightarrow{H_2O} OH{\cdot}X{\cdot}CHO + CH_3{\cdot}NH_2$$

This suggestion of isomerisation was based on the explanation given by Sommelet (*Compt. rend.*, 1913, **157**, 854) for the formation of benzaldehyde in a reaction between benzyl chloride and hexamine. Angyal and Rassack (*J.*, 1949, 2700) have recently examined the Sommelet

reaction and in the light of their results the present authors decided to investigate the reactions between phenols and hexamine under new conditions.

In their investigation Angyal and Rassack, while emphasising a dehydrogenation mechanism, limited their experimental evidence to reactions in aqueous conditions. For this reason they ascribe the dehydrogenation function of hexamine to its hydrolysis products, with special reference to the hydrolysis fragment, $CH_2{:}NH$. In one example they heated dibenzylamine in acetic acid with hexamine and aqueous formaldehyde solution and obtained benzaldehyde. As this reaction had a bearing on our investigation we have re-examined it and find it proceeds more readily when the dibenzylamine is heated with hexamine in glacial acetic acid. Subsequent hydrolysis gave benzaldehyde and benzylamine at once. The ease with which this reaction proceeds led us to the view that phenolic aldehydes might arise from the hydrolysis of phenolic Schiff's bases which had been formed from phenolic secondary amines by the dehydrogenating action of hexamine.

Few phenolic secondary amines of the form $OH{\cdot}X{\cdot}CH_2{\cdot}NH{\cdot}CH_2{\cdot}X{\cdot}OH$ ($H{\cdot}X{\cdot}OH$ = a phenol) have been previously recorded. Zinke *et al.* (*Monatsh.*, 1948, **78**, 311; 1949, **80**, 148) described the preparation of secondary amines of this type by heating hexamine with a phenol at 130°. They applied this reaction successfuly only to 2 : 4-dimethyl- and 2 : 4-dichloro-phenol. From the other two phenols they tested, 3 : 4-dimethyl- and *p-tert.*-butyl-phenol, the resulting amines were complex, the molecules containing at least four phenol nuclei linked by $-CH_2{\cdot}NH{\cdot}CH_2-$ bridges. They did not try the further action of hexamine on the secondary amines. Hultzsch (*Chem. Ber.*, 1949, **82**, 16) described the preparation of secondary amines from 2 : 4-dimethyl- and 2-methyl-4-*tert.*-butyl-phenol by heating them with hexamine and water. This method involves separation of the secondary amine from resinous products. He also described the formation of the secondary amines mixed with tertiary amines when the phenol is heated with hexamine until the temperature was 180°. Hultzsch did not describe the further action of hexamine on the secondary amines.

Duff and Bills (*J.*, 1934, 1307) obtained a Schiff's base directly from β-naphthol and hexamine in acetic acid and by hydrolysis of the base separated 2-hydroxy-1-naphthaldehyde and 2-hydroxy-1-naphthylmethylamine. The secondary amine which probably gave rise to the Schiff's base was not observed. Acetic acid was found to be an unsuitable medium for obtaining Schiff's bases from other phenols. Since boric acid had proved useful in glycerol for preparing phenolic aldehydes the present authors decided to use boric acid in other non-aqueous media and found a suitable solvent in 2-ethoxyethanol. Boric anhydride was also tried in many experiments but only in the reaction involving *m*-xylenol did it offer advantages over boric acid. Metaboric acid proved unsuitable owing to its low solubility. In the absence of boric acid the reactions between phenols and hexamine were too complex. In the presence of boric acid the reactions proceeded on simpler lines.

Eleven phenols ($H{\cdot}X{\cdot}OH$) were used in this investigation and from each a secondary amine $OH{\cdot}X{\cdot}CH_2{\cdot}NH{\cdot}CH_2{\cdot}X{\cdot}OH$ and a Schiff's base $OH{\cdot}X{\cdot}CH{:}N{\cdot}CH_2{\cdot}X{\cdot}OH$ were obtained. All the amines are new and were obtained crystalline. They are not hydrolysed on boiling in alcohol with hydrochloric acid. When heated in acetic acid with hexamine they yielded yellow Schiff's bases. When the Schiff's bases were hydrolysed in alcohol with hydrochloric acid it was expected the results would be in accordance with the equation

$$OH{\cdot}X{\cdot}CH{:}N{\cdot}CH_2{\cdot}X{\cdot}OH + H_2O + HCl \longrightarrow OH{\cdot}X{\cdot}CHO + OH{\cdot}X{\cdot}CH_2{\cdot}NH_2{,}HCl$$

However this only applied to the Schiff's bases from β-naphthol and 4-chloro-3 : 5-dimethyl-phenol. All the other Schiff's bases on hydrolysis yielded a phenolic aldehyde and, in place of the expected primary amine, the original secondary amine and ammonium chloride. This may have occurred either by the reaction

$$OH{\cdot}X{\cdot}CH_2{\cdot}NH_2 + OH{\cdot}X{\cdot}CH_2{\cdot}NH_2{,}HCl \longrightarrow OH{\cdot}X{\cdot}CH_2{\cdot}NH{\cdot}CH_2{\cdot}X{\cdot}OH + NH_4Cl$$

or by reaction of the primary amine with the Schiff's base :

$$OH{\cdot}X{\cdot}CH_2{\cdot}NH_2 + OH{\cdot}X{\cdot}CH{:}N{\cdot}CH_2{\cdot}X{\cdot}OH + H_2O \longrightarrow OH{\cdot}X{\cdot}CHO + OH{\cdot}X{\cdot}CH_2{\cdot}NH{\cdot}CH_2{\cdot}X{\cdot}OH + NH_3$$

The identity of the secondary amine formed in each case was established by analysis and by reconversion into the Schiff's base and thence into the aldehyde by hydrolysis. All the Schiff's bases yielded the phenolic aldehydes which were produced by the glyceroboric acid method (Duff, *loc. cit.*) except in the case of the Schiff's base derived from 4-chloro-3-methylphenol.

The aldehyde which was obtained in this case was the new aldehyde, 4-chloro-2-formyl-3-methylphenol (I), thus indicating that the Schiff's base which yielded it had the structure (II).

(I.)

(II.)

The aldehyde formed from 4-chloro-3-methylphenol in the glyceroboric acid reaction is the other *o*-aldehyde. The identity of the 2-aldehyde was established by oxidation of the methyl ether to a chloro-methoxyphthalic acid which yielded a phthalein with phenol. In all cases where an *o*-hydroxy-aldehyde was separated by steam-distillation the residual liquors were tested for the presence of *p*-hydroxy-aldehydes with negative results. The only *p*-hydroxy-aldehyde obtained came from α-naphthol which yielded 4-hydroxy-1-naphthaldehyde from hydrolysis of the Schiff's base, together with some of the secondary amine and ammonium chloride.

Experimental.

All m. p.s are uncorrected.

Preparation of Secondary Amines.—The phenol (10 g.) and boric acid (4 g.) were dissolved in boiling 2-ethoxyethanol (40 ml.). Hexamine (5 g.) was then added and the solution boiled under reflux for 2 hours and cooled. The method of extraction varied with the nature of the phenol:

(a) *From phenol and cresols.* The reaction mixture was filtered and poured into 150 ml. of water. The resultant oil was washed with water by decantation and left overnight with water. It was then separated and stirred with cold alcohol, and the residual solid was recrystallised from aqueous alcohol.

Phenol yielded *di-o-hydroxybenzylamine* (2·5 g.) as a micro-crystalline white powder, m. p. 190—200° (decomp.) [Found: C, 73·4; H, 6·2; N, 6·0%; *M* (Rast), 240. $C_{14}H_{15}O_2N$ requires C, 73·4; H, 6·5; N, 6·1%; *M*, 229]. Crystals of a *hydrochloride* were obtained from a solution of the base in warm concentrated hydrochloric acid (Found: HCl, 13·8. $C_{14}H_{15}O_2N$,HCl requires HCl, 13·75%).

o-Cresol yielded *di-(2-hydroxy-3-methylbenzyl)amine* (5·1 g.), m. p. 150—155° (decomp.) [Found: C, 74·9; H, 7·4; N, 5·2%; *M* (Rast, 265. $C_{16}H_{19}O_2N$ requires C, 74·7; H, 7·4; N, 5·4%; *M*, 257].

m-Cresol yielded *di-(2-hydroxy-4-methylbenzyl)amine* (7·5 g.), m. p. 150—157° (decomp.) [Found: C, 74·1; H, 7·4; N, 5·3%; *M* (Rast), 270.

p-Cresol yielded *di-(2-hydroxy-5-methylbenzyl)amine* (7·7 g.), m. p. (anhyd.) 168—170° (decomp.) [Found: C, 69·2; H, 7·2; N, 5·1; H_2O, 6·8%; *M* (Rast), 275. $C_{16}H_{19}O_2N,H_2O$ requires C, 69·8; H, 7·6; N, 5·1; H_2O, 6·6%; *M*, 275]. Crystals of a *hydrochloride* were obtained by passing hydrogen chloride through a solution of the base in alcohol (Found: HCl, 12·4%).

(b) *From p-chlorophenol and 4-chloro-3-methylphenol.* The reaction mixture was poured into 150 ml. of water. The oil which separated was washed with water by decantation and then stirred with ether. The residual solid was recrystallised from alcohol.

p-Chlorophenol yielded *di-(2-hydroxy-5-chlorobenzyl)amine* (2·8 g.), m. p. 155—160° (decomp.) [Found: C, 56·1; H, 4·2; N, 4·9%; *M* (Rast), 295. $C_{14}H_{13}O_2NCl_2$ requires C, 56·3; H, 4·3; N, 4·7%; *M*, 298]. Crystals of a *hydrochloride* were obtained by passing hydrogen chloride through a solution of the base in alcohol and hydrochloric acid (Found: HCl, 11·0. $C_{14}H_{13}O_2NCl_2$,HCl requires HCl, 10·9%).

4-Chloro-3-methylphenol yielded *di-(2-hydroxy-5-chloro-6-methylbenzyl)amine* (5·5 g.), m. p. 185—190° (decomp.) [Found: C, 58·8; H, 5·1; N, 4·35%; *M* (Rast), 340. $C_{16}H_{17}O_2NCl_2$ requires C, 58·9; H, 5·2; N, 4·3%; *M*, 326]. Crystals of a *hydrochloride* were obtained on addition of concentrated hydrochloric acid to a solution of the base in hot acetic acid (Found: HCl, 9·9. $C_{16}H_{17}O_2NCl_2$,HCl requires HCl, 10·0%).

(c) *From β-naphthol, 4-chloro-3:5-dimethylphenol, and 4-hydroxydiphenyl.* The reaction mixture was poured into 150 ml. of water and set aside overnight. The solid was collected. The β-naphthol compound was washed with boiling alcohol and recrystallised from aqueous acetone; the 4-chloro-3:5-dimethylphenol compound was washed with water and recrystallised from aqueous alcohol; the 4-hydroxydiphenyl compound was washed with warm acetone and recrystallised from alcohol. The following were prepared.

Di-(2-hydroxy-1-naphthylmethyl)amine (6·1 g.), m. p. 170—178° (decomp.) [Found: C, 80·2; H, 6·1; N, 4·0%; *M* (Rast), 325. $C_{22}H_{19}O_2N$ requires C, 80·2; H, 5·8; N, 4·2%; *M*, 329]; *hydrochloride* formed by hydrochloric acid in warm 2-ethoxyethanol (Found: HCl, 10·2. $C_{22}H_{19}O_2N$,HCl requires HCl, 10·0%).

Di-(3-chloro-6-hydroxy-2:4-dimethylbenzyl)amine (6·8 g.), m. p. 219° (decomp.) [Found: C, 61·2; H, 6·2; N, 3·95%; *M* (Rast), 335. $C_{18}H_{21}O_2NCl_2$ requires C, 61·0; H, 5·95; N, 3·95%; *M*, 354]; *hydrochloride*, obtained in acetic acid (Found: HCl, 9·3. $C_{18}H_{21}O_2NCl_2$,HCl requires HCl, 9·3%).

Di-(2-hydroxy-5-phenylbenzyl)amine (5 g.), m. p. 195—200° (decomp.) [Found: C, 82·3; H, 6·05; N, 3·5%; *M* (Rast), 370. $C_{26}H_{23}O_2N$ requires C, 81·9; H, 6·05; N, 3·7%; *M*, 381]; *hydrochloride*, obtained in acetic acid (Found: HCl, 8·6. $C_{26}H_{23}O_2N$,HCl requires HCl, 8·7%).

(d) *From m-5-xylenol.* Boric anhydride (2 g.) was used in place of boric acid, and a smaller amount of hexamine (2·5 g.) and a larger amount of solvent (50 ml.) were added. The cooled reaction mixture

was poured into water (150 ml.), and the solid which precipitated was collected and washed with alcohol. The amine could only be obtained pure as the hydrochloride. This separated from a solution of the base in warm 2-ethoxyethanol and concentrated hydrochloric acid on cooling. *Di-(2-hydroxy-4 : 6-dimethylbenzyl)amine hydrochloride* (4·5 g.) had m. p. 215—220° (decomp.) [Found : C, 66·7; H, 7·5; N, 4·0; HCl, 11·4%; *M* (Rast), 310. $C_{18}H_{23}O_2N$,HCl requires C, 67·1; H, 7·4; N, 4·4; HCl, 11·4%; *M*, 321·5].

(e) *From α-naphthol.* 2-Methoxyethyl acetate (50 ml.) was used in place of 2-ethoxyethanol. Recrystallisation from aqueous alcohol yielded *di-(4-hydroxy-1-naphthylmethyl)amine* (4·7 g.), a pale yellow powder, m. p. 205° (decomp.) [Found : C, 80·2; H, 5·5; N, 4·1%; *M* (Rast), 335. $C_{23}H_{19}O_2N$ requires C, 80·2; H, 5·8; N, 4·2%; *M*, 329]; the *hydrochloride* was obtained in glacial acetic acid (Found : HCl, 10·1. $C_{23}H_{19}O_2N$,HCl requires HCl, 10·[illegible]%).

Preparation of Schiff's Bases.—The secondary am[illegible] g.) and hexamine (5 g.) were heated in acetic acid (15 ml.) on a boiling water-bath for the peri[illegible]ated below. The solutions were then strongly coloured, and in most cases showed a marked gre[illegible]orescence when cold. The solution was filtered and poured into sufficient water to give complet[illegible] precipitation (15—30 ml.). The solid was collected immediately and washed with water, except for the compounds from phenol, *m*-5-xylenol, and α-naphthol which were washed with dilute hydrochloric acid. The Schiff's bases from phenol, the cresols, and *m*-xylenol were too soluble and too readily hydrolysed to be recrystallised. The other bases were recrystallised from the aqueous alcohol. The following were prepared.

2-Hydroxy-N-2'-hydroxybenzylidenebenzylamine (1·2 g.), a bright yellow powder (after 16 hours' heating) (Found : C, 73·5; H, 5·9; N, 6·4. $C_{14}H_{13}O_2N$ requires C, 74·0; H, 5·7; N, 6·2%); *2-hydroxy-N-(2-hydroxy-3-methylbenzylidene)-3-methylbenzylamine* (3·8 g.), an orange powder (after 9 hours' heating) (Found : C, 75·5; H, 6·4; N, 5·45. $C_{16}H_{17}O_2N$ requires C, 75·3; H, 6·7; N, 5·5%); *2-hydroxy-N-(2-hydroxy-4-methylbenzylidene)-4-methylbenzylamine* (2·7 g.), a bright yellow powder (after 9 hours' heating) (Found : C, 75·4; H, 6·8; N, 5·6%); *2-hydroxy-N-(2-hydroxy-5-methylbenzylidene)-5-methylbenzylamine* (3·5 g.), a bright yellow powder (after 9 hours' heating) (Found : C, 75·9; H, 7·0; N, 5·5%); *5-chloro-2-hydroxy-N-(5-chloro-2-hydroxybenzylidene)benzylamine* (4·2 g.), a yellow powder (after 6 hours' heating) (Found : C, 57·0; H, 4·1; N, 4·5. $C_{14}H_{11}O_2NCl_2$ requires C, 56·8; H, 3·7; N, 4·7%); *3-chloro-6-hydroxy-N-(3-chloro-6-hydroxy-2-methylbenzylidene)-2-methylbenzylamine* (3·7 g.), a bright yellow powder (after 6 hours' heating) (Found : C, 59·5; H, 4·8; N, 4·4. $C_{16}H_{15}O_2NCl_2$ requires C, 59·3; H, 4·65; N, 4·35%); 2-hydroxy-1-naphthyl-*N*-(2-hydroxy-1-naphthylmethylene)methylamine (4·5 g.) (after 2 hours' heating) (Found : N, 4·3. Calc. for $C_{22}H_{17}O_2N$: N, 4·3%); *3-chloro-N-(3-chloro-6-hydroxy-2 : 4-dimethylbenzylidene)-6-hydroxy-2 : 4-dimethylbenzylamine* (3·7 g.), an orange-yellow powder (after 6 hours' heating) (Found : C, 61·2; H, 5·7; N, 4·3. $C_{18}H_{19}O_2NCl_2$ requires C, 61·3; H, 5·4; N, 4·0%); *2-hydroxy-N-(2-hydroxy-5-phenylbenzylidene)-5-phenylbenzylamine* (4·9 g.), a bright yellow powder (after 6 hours' heating) (Found : C, 82·3; H, 5·7; N, 3·5. $C_{26}H_{21}O_2N$ requires C, 82·3; H, 5·55; N, 3·7%); (from the hydrochloride of the secondary amine) *2-hydroxy-N-(2-hydroxy-4 : 6-dimethylbenzylidene)-4 : 6-dimethylbenzylamine* (2·0 g.), a bright yellow powder (after 2 hours' heating) (Found : C, 75·5; H, 7·5; N, 5·5. $C_{18}H_{21}O_2N$ requires C, 76·3; H, 7·4; N, 4·95%); and *4-hydroxy-N-(4-hydroxy-1-naphthylmethylene)-1-naphthylmethylamine* (4·3 g.), a yellow powder (after 2 hours' heating) (Found : C, 80·4; H, 5·3; N, 4·2. $C_{22}H_{17}O_2N$ requires C, 80·7; H, 5·2; N, 4·3%).

Hydrolysis of Schiff's Bases.—The Schiff's base (2 g.) was heated with 20 ml. of a mixture of equal volumes of alcohol and hydrochloric acid (*d* 1·17). When the mixture had reached the b. p. it was filtered and the filtrate was steam-distilled until no more aldehyde was obtained. For the α-naphthol compound, the solution was extracted with ether instead of being distilled. In most cases some solid amine hydrochloride separated from the still residue on concentration and cooling. With *o*- and *m*-cresol, there was no separation owing to the high solubility of the hydrochlorides, and the free bases were obtained by neutralising the solution. The amine in each case was filtered off and examined and the filtrate tested for aldehydes and ammonium chloride. The following aldehydes were obtained, together with secondary amine and ammonium chloride.

Salicylaldehyde (0·6 g.) (phenylhydrazone, m. p. 142°); 2-hydroxy-3-methylbenzaldehyde (0·3 g.) (phenylhydrazone, m. p. 92°); 2-hydroxy-4-methylbenzaldehyde (0·6 g.), m. p. and mixed m. p. 59°; 2-hydroxy-5-methylbenzaldehyde (0·45 g.), m. p. and mixed m. p. 56°; 5-chloro-2-hydroxybenzaldehyde (0·5 g.), m. p. and mixed m. p. 99·5°; *4-chloro-2-formyl-3-methylphenol* (0·6 g.), m. p. 100·5° (Found : C, 55·7; H, 4·4. $C_8H_7O_2Cl$ requires C, 56·3; H, 4·1%) [methylation with methyl sulphate and then oxidation with potassium permanganate afforded a dibasic acid (Found : equiv., 119. Calc. for $C_9H_7O_4Cl$: equiv., 116) which gave a phthalein reaction with phenol, thus confirming that the aldehyde group was *ortho* to the methyl group]; 2-hydroxy-1-naphthaldehyde (0·7 g.), m. p. and mixed m. p. 82° [with 2-hydroxy-1-naphthylmethylamine hydrochloride (Duff, *J.*, 1934, 1307)]; 4-chloro-2-formyl-3 : 5-dimethylphenol (0·4 g.), m. p. and mixed m. p. 95° [with *3-chloro-6-hydroxy-2 : 4-dimethylbenzylamine hydrochloride*, a microcrystalline white powder (Found : C, 48·9; H, 5·8; N, 6·6; HCl, 16·3. $C_9H_{12}ONCl,HCl$ requires C, 48·7; H, 5·8; N, 6·3; HCl, 16·4%]; 3-formyl-4-hydroxydiphenyl (0·3 g.), m. p. and mixed m. p. 102°; 4-formyl-3 : 5-dimethylphenol (0·15 g.), m. p. and mixed m. p. 49°; and 4-hydroxy-1-naphthaldehyde (0·1 g.), m. p. 180°.

Reaction with Dibenzylamine.—Dibenzylamine (5 g.) and hexamine (1 g.) were heated in glacial acetic acid (10 ml.) for 5 minutes at the b. p. The solution became deep yellow. Dilute hydrochloric acid was added and the mixture was steam-distilled. Benzaldehyde (1·2 g.) was obtained. The residue was treated with toluene-*p*-sulphonyl chloride and yielded toluene-*p*-sulphonbenzylamide, m. p. and mixed m. p. 115°

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347. *Substituted Benzidines and Related Compounds as Reagents in Analytical Chemistry. Part VI.* The Precipitation of Tungsten.*

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The tungsten-precipitating properties of benzidine, diphenyline, and certain substituted benzidines, and related compounds have been examined. It was found that 1-amino-4-*p*-aminophenylnaphthalene precipitated tungsten quantitatively from acid solution and gave a complete separation from molybdenum.

The amines described in previous papers in this series have been examined as precipitants for tungsten (in the form of tungstate). Benzidine has been used for this purpose for many years, but does not appear to have achieved wide usage, possibly because of its non-selectivity. Some further tests on benzidine have therefore now been carried out to check the accuracy of the method, and to find to what extent molybdenum (as molybdate) is coprecipitated. To complete the investigation, an examination of diphenyline as a reagent for tungsten has been made. This reagent was proposed by Feigl (*Rec. Trav. chim.*, 1939, **58**, 471) for the detection of tungsten in the presence of molybdenum, since in acid solution up to 10% of molybdenum did not interfere, but no attempt appears to have been made to apply the reaction quantitatively. Unlike benzidine sulphate, diphenyline sulphate is soluble.

Determination of Tungsten (as Tungstate), Benzidine being used as Reagent.—When tungsten was precipitated from neutral solution, full recovery was obtained under the conditions used. Molybdenum behaved similarly. However, at an acidity of 0·5N. in hydrochloric acid, only about a 90% recovery of tungsten was obtained. Under the same conditions, molybdenum was not appreciably precipitated. When mixtures of tungsten and molybdenum were precipitated at this same acidity, the results obtained indicated appreciable coprecipitation of molybdenum, and this was confirmed by applying the thiocyanate test to the residue obtained on ignition of the precipitate. Hence, it is impossible to separate these elements quantitatively by adjustment of the acidity. The results obtained are summarised below.

Precipitation of tungsten and molybdenum by benzidine from neutral and from acid solutions.

W present (mg.).	Mo present (mg.).	W found (mg.). Final acidity: 0.	W found (mg.). Final acidity: 0·5N.	Mo found (mg.). Final acidity: 0.	Mo found (mg.). Final acidity: 0·5N.
75	—	74·9, 75·1	68·1, 67·5	—	—
—	65	—	—	64·9, 65·0	0·3, 0·1
75	65	—	72·3, 72·9	—	—

It is well known that molybdenum forms strong complexes with oxalic acid, but we were unable to find any reference to similar complex formation with tungsten. Some experiments in which sufficient oxalic acid was added to form the complex with molybdenum showed that tungsten also forms a complex, for recoveries of less than 5% were obtained, as seen from the following results.

Precipitation of tungsten and molybdenum by benzidine from oxalic acid solution.

W present (mg.).	Mo present (mg.).	W found (mg.).	Mo found (mg.).
75	—	3·2, 3·0	—
—	65	—	1·3, 1·0
75	65	4·4, 3·9	—

Precipitation of Tungsten with Diphenyline.—When tungsten was precipitated from neutral solution with diphenyline, full recovery was obtained. When, however, precipitations were effected at acidities of 0·1N., 0·2N., and 0·3N. with respect to hydrochloric acid, the recoveries were less than 80%. When the filtrates from the 0·3N-acid precipitations were evaporated to dryness on the water-bath, redissolved in water, and treated with benzidine, almost all of the unprecipitated tungsten was recovered. Molybdenum was precipitated completely in neutral

* Part V, *J.*, 1951, 550.

solution, but it was evident that the recovery of tungsten in slightly acid solution was not sufficiently satisfactory to warrant further examination. Results are shown below.

Precipitation of tungsten by diphenyline from neutral and acid solution.

W present (mg.).	Precipitation storage time.	W found (mg.). Final acidity: 0.	0·1N.	0·2N.	0·3N.
75	½ hour	74·7, 74·6	—	—	—
75	1 hour	74·9, 74·9	59·9, 58·7	58·8, 58·7	57·8, 57·7
75	2 hours	74·9, 74·9	59·8, 59·9	59·2, 59·4	57·7, 58·2
75	Overnight	—	59·7, 60·0	59·1, 59·4	59·2, 58·8

Precipitation of Tungsten with Various Amines.—The amines described in previous papers were next examined as precipitants for tungsten, since a reagent which would precipitate tungsten from an acid solution is desirable. Hence, in order to test the precipitating properties of our amines, precipitation was effected at a final acidity of 1N. with respect to hydrochloric acid. The results are listed below.

Precipitation of tungsten by certain substituted benzidines and related compounds from acid solution.

Amine.	W present (mg.).	W found (mg.).	Amine.	W present (mg.).	W found (mg.).
2-Methylbenzidine.....	15	9·9, 10·3	4-Aminodiphenyl	15	7·7, 6·3
3-Methylbenzidine.....	15	2·1, 3·9	1-Amino-4-*p*-aminophenyl-naphthalene	15	14·7, 14·8
2 : 2′-Dimethylbenzidine ...	15	4·8, 6·2	2-Aminodiphenylamine ...	15	8·3, 8·1
2 : 3′-Dimethylbenzidine ...	15	6·2, 5·6	4-Aminodiphenylamine ...	15	1·7, 3·5
3 : 3′-Diethylbenzidine ...	15	2·3, 2·6	4 : 4′-Diaminostilbene	15	14·6, 14·5
3 : 3′-Diaminobenzidine ...	15	5·1, 3·9			
2-Aminodiphenyl	15	3·5, 3·7			

The tests were repeated in the presence of sulphuric acid to assist in the formation of more granular precipitates, but similar results were obtained.

Only two amines, 4 : 4′-diaminostilbene and 1-amino-4-*p*-aminophenylnaphthalene, gave results of sufficient promise to warrant further investigation.

Precipitation of Tungsten with 4 : 4′-Diaminostilbene.—In neutral solution both tungsten and molybdenum were precipitated quantitatively. At a final acidity of 0·7N. with regard to hydrochloric acid, tungsten was almost quantitatively precipitated. The amount of tungsten remaining in solution might be disregarded for certain types of industrial analysis, but, unfortunately, occasional inexplicable low results were obtained, even after the precipitates had been kept overnight. Various amounts of tungsten were determined, but in nearly every case the results were slightly, and in some cases considerably, low.

Molybdenum yielded no precipitate at all at an acidity of 0·7N. When tungsten was determined in its presence, there was no coprecipitation at this acidity. The acidity was reduced to 0·5N., but the results for tungsten were still slightly low, and, when molybdenum was present under the same conditions, appreciable coprecipitation occurred. Results are included in the following table.

Precipitation of tungsten and molybdenum by 4 : 4′-diaminostilbene from neutral and from acid solution.

W present (mg.).	Mo present (mg.).	Pptn. storage time, (hrs.).*	W found (mg.). Final acidity. 0.	0·5N.	0·7N.	Mo found (mg.). Final acidity: 0.	0·5N.
15	—	2	14·9, 15·1	14·9, 14·9	14·7, 14·4	—	—
15	—	2	14·9, 15·0	14·9, 14·8	13·9, 14·8	—	—
15	—	N	—	—	14·9, 14·5	—	—
15	—	N	—	—	13·6, 14·8	—	—
—	13	2	—	—	—	12·9, 13·0	0, 0
—	13	2	—	—	—	12·8, 12·9	0·1, 0
15	13	N	—	14·9, 15·5	14·8, 13·8	—	—
15	13	N	—	15·5, 15·6	14·7, 14·9	—	—
7·5	—	N	—	—	7·4, 6·9	—	—
7·5	—	N	—	—	7·2, 7·4	—	—
3·8	—	N	—	—	3·5, 3·0	—	—
3·8	—	N	—	—	3·5, 3·4	—	—

* N = Overnight.

Several expedients were tried to overcome the slight loss of tungsten, such as adding paper pulp, reducing the volume of the solution as far as was compatible with that likely to be used in practice, and washing the precipitate both with reagent and with wash solution saturated with precipitate, but no improvement could be observed. The addition of paper pulp, however, gave a more easily filterable precipitate.

Oxidising agents (but not Fe^{3+}) interfered.

Precipitation of Tungsten with 1-*Amino*-4-p-*aminophenylnaphthalene.*—Both tungsten and molybdenum were precipitated quantitatively from neutral solution. At an acidity 0·7N. with respect to hydrochloric acid, tungsten was precipitated almost quantitatively but molybdenum gave no precipitate. When tungsten was precipitated in the presence of molybdenum at an acidity of 0·7N., no coprecipitation occurred. At an acidity of 0·5N., however, there was a slight coprecipitation of molybdenum. High results were obtained and molybdenum was detected in the precipitate by the thiocyanate test. At an acidity of 1N., the results for tungsten were similar to those obtained in 0·7N-solution, but, when the volume was increased at this acidity to 150 ml. and 200 ml., low results were obtained. It is recommended, then, that a volume of 100 ml. or less and an acid concentration of 0·7N. be used to obtain virtually complete precipitation.

When hydrochloric acid alone was used as the wash liquid the results were always slightly lower than when it was saturated with the precipitate.

The effect of varying the storage time at an acidity of 1N. was examined. After 4 hours the results were always low, but after storage overnight, precipitation was virtually complete. The results are always slightly low but the slight error involved may possibly be ignored for most types of analysis, especially when it is considered that a complete separation from molybdenum is obtained. Results are included in the following table.

Precipitation of tungsten and molybdenum by 1-*amino*-4-p-*aminophenylnaphthalene from neutral and from acid solution.*

W present (mg.).	Mo present (mg.).	Pptn. storage time (hrs.).*	Final vol. (ml.).	W found (mg.). Final acidity: 0.	0·5N.	0·7N.	1N.
15	—	½	70	14·8, 14·9	—	—	11·4
				14·8, 14·8	—	—	10·8, 10·5
15	—	1	70	14·9, 15·0	—	—	11·1, 11·6
				15·0, 14·9	—	—	11·7
15	—	2	70	—	—	—	12·6, 12·9
				—	—	—	13·0
15	—	4	70	—	—	—	13·2, 13·7
				—	—	—	13·4
15	—	N	70	—	—	—	14·9, 14·8
				—	—	—	14·9
7·5	—	N	70	—	—	7·4, 7·5	7·3, 7·4
				—	—	7·4, 7·4	7·4, 7·3
3·8	—	N	70	—	—	3·6, 3·6	3·5, 3·4
				—	—	3·5, 3·7	3·7, 3·6
—	13†	1 (for neutral)	70	13·0, 12·9	0, 0	0, 0	}
		N (for acid)		12·9, 13·0	0 0	0 0	}
15	13	N	70	—	—	14·8, 14·8	14·8, 14·9
				—	15·3, 15·2	14·9, 15·0	14·9, 14·8
				—	15·6, 15·6	14·9, 14·8	14·9, 15·0
				—	—	14·9, 14·9	14·9, 14·8
15	—	N	100	—	—	—	14·8, 14·8
				—	—	—	14·7, 14·8
15	—	N	150	—	—	—	14·6, 14·7
				—	—	—	14·7, 14·6
15	—	N	200	—	—	—	14·6, 14·6
				—	—	—	14·5, 14·7

* N = Overnight. † Results in cols. 5, 6 and 7 are for Mo (mg.).

Under the conditions employed in the precipitation, oxidising agents and Fe^{3+}, which gave a blue-green precipitate with the reagent, interfered; Fe^{2+} did not interfere, nor did the following ions, which were selected from the various analytical groups: Cu^{2+}, Cd^{2+}, Al^{3+}, Cr^{3+}, Ni^{2+}, Zn^{2+}, Ca^{2+}, Mg^{2+}, Na^{+}, K^{+}.

Experimental.*

Solutions required.—Tungsten solution. Prepared by fusing pure tungstic oxide with sodium carbonate at 800°, dissolving the melt in distilled water, and neutralising to methyl-red with hydrochloric acid.

Molybdate solution. Prepared by dissolving recrystallised sodium molybdate in distilled water.

Reagents. These were prepared by dissolving the stated quantity of the corresponding hydrochloride in 100 ml. of distilled water: benzidine, 1 g.; diphenyline, 1 g.; amines, 0·5 g.; 4 : 4′-diaminostilbene, 0·5 g.; 1-amino-4-*p*-aminophenylnaphthalene, 1 g.

I. *Precipitation with Benzidine.*—(1) *Neutral solution* (see table, p. 1516). (i) Tungsten. 20 Ml. of benzidine reagent were added to 50 ml. of neutral tungstate solution. After 2 hours, the precipitate was filtered through a pulp pad, washed with a 5% solution of the reagent, and ignited in a platinum crucible at 750°; the residue was weighed as WO_3.

(ii) Molybdenum. 20 Ml. of benzidine reagent were added to 50 ml. of neutral molybdate solution; after the same procedure as in (i), ignition in a platinum crucible at 500° afforded MoO_3.

(2) *Acid solution* (see table, p. 1516). (i) Tungsten. 20 Ml. of benzidine reagent were added to 50 ml. of acid tungstate solution, the final acidity of the solution being 0·5N. to hydrochloric acid. The liquor was kept overnight and the procedure was then as in (1)(i).

(ii) Molybdenum. 20 Ml. of benzidine reagent were added to 50 ml. of acid molybdate solution, the final acidity of the solution being 0·5N. to hydrochloric acid. The solution was kept overnight, and then treated as in (1)(ii).

(iii) Tungsten + molybdenum. 20 Ml. of benzidine reagent were added to 50 ml. of acid tungstate + molybdate solution, the final acidity of the solution being 0·5N. Next morning, the precipitate was treated as in (1)(ii), the residue being weighed as WO_3.

(3) *Oxalic acid solution* (see table, p. 1516). These experiments were carried out as for I(2) but in neutral solution to which 1 g. of oxalic acid had been added.

II. *Precipitation with Diphenyline* (see table, p. 1517).—(1) *Neutral solution.* (i) Tungsten. As for I(1), but with 20 ml. of diphenyline reagent as precipitant and various times.

(2) *Acid solution.* (i) Tungsten. As for I(2), but with 20 ml. of diphenyline reagent as precipitant, and with final acidities 0·1N., 0·2N., and 0·3N. with respect to hydrochloric acid.

III. *Precipitation with Substituted Benzidines and Related Compounds* (see table, p. 1517).—20 Ml. of amine reagent were added to 50 ml. of acid tungstate solution, the final acidity of the solution being 1N. with regard to hydrochloric acid. A small amount of paper pulp was added, and after being kept overnight, the precipitate was filtered through a pulp pad, washed with a 5% solution of the reagent, ignited in a platinum crucible at 750°, and weighed as WO_3.

IV. *Precipitation with 4 : 4′-Diaminostilbene* (see table, p. 1517).—(1) *Neutral solution.* (i) Tungsten. Procedure was as for I(1), but with 20 ml. of 4 : 4′-diaminostilbene reagent as precipitant.

(ii) Molybdenum. As for I(1), but with 20 ml. of 4 : 4′-diaminostilbene reagent as precipitant.

(2) *Acid solution.* (i) Tungsten. As for I(2), but with 20 ml. of 4 : 4′-diaminostilbene reagent as precipitant. The final acidities were 0·5N. and 0·7N. with respect to hydrochloric acid.

(ii) Molybdenum. As for I(2), but with 20 ml. of 4 : 4′-diaminostilbene reagent. The final acidity was 0·5N. with regard to hydrochloric acid.

(iii) Tungsten + molybdenum. As for I(2), but with 20 ml. of 4 : 4′-diaminostilbene reagent. The final acidities were 0·5N. and 0·7N. with respect to hydrochloric acid.

V. *Precipitation with 1-Amino-4-p-aminophenylnaphthalene* (see table, p. 1518).—(1) *Neutral solution.* (i) Tungsten. Procedure as for I(1), but with 20 ml. of the reagent as precipitant. Paper pulp was added to the solution, and to the solutions referred to in the following paragraphs, to give a more easily filterable precipitate. The precipitate was kept for ½ or for 1 hour.

(ii) Molybdenum. The procedure was similar to that in I(i). The precipitate was set aside for 1 hour.

(2) *Acid solution.* (i) Tungsten. Procedure as for I(2), with 20 ml. of reagent. The tungstate solution contained varying amounts of tungsten. Times, final acidities, and final volumes at an acidity of 1N. to hydrochloric acid were varied.

(ii) Molybdenum. Procedure was similar to that in I(2).

(iii) Tungsten + molybdenum. Procedure was as for I(2), 20 ml. of reagent solution being used.

Our thanks are offered to Mr. B. Bagshawe, Brown-Firth Research Laboratories, Sheffield, for supplying pure tungstic oxide, and for his many helpful suggestions during the course of this work. We also thank the Director of Research, May and Baker, Ltd., for gifts of diaminostilbene and dinitrostilbene.

Chemistry Department, The University, Birmingham, 15. [*Received, December 13th*, 1950.]

* The weights of tungsten and molybdenum in each test solution are given in the corresponding tables.

348. *Substituted Benzidines and Related Compounds as Reagents in Analytical Chemistry. Part VII.* 3 : 3′-Dimethylnaphthidine as Indicator in the Titration of Zinc with Ferrocyanide.*

By R. Belcher, A. J. Nutten, and W. I. Stephen.

The properties of 3 : 3′-dimethylnaphthidine (4 : 4′-diamino-3 : 3′-dimethyl-1 : 1′-dinaphthyl) as an indicator in the titration of zinc with ferrocyanide have been investigated. It is more sensitive than naphthidine and the end-point can be detected readily even when 0·001M-solutions are used for the titration.

It has recently been shown (Belcher and Nutten, *J.*, 1951, 547) that naphthidine can be used as an indicator when zinc is determined by titration with potassium ferrocyanide. Since it seemed probable that *m*-substituted naphthidines would behave likewise, the indicator properties of 3 : 3′-dimethylnaphthidine (for preparation, see Fries and Lohmann, *Ber.*, 1921, **54**, 2922) have been investigated. The colour change at the end-point when 0·001M-solutions were used was equivalent in intensity to that obtained with naphthidine when 0·01M-solutions were used; hence it appears to be ten times as sensitive. Moreover, 3 : 3′-dimethylnaphthidine appears to be more stable in solution than both naphthidine and *o*-dianisidine, for the end-point colours obtained with the last two indicators fade after a few hours, whereas that with 3 : 3′-dimethylnaphthidine only shows signs of fading after a few days.

When the zinc and ferrocyanide solutions were diluted to less than 0·01M., it was found necessary to dilute the other requisite reagents (sulphuric acid, ammonium sulphate, and potassium ferricyanide) in order to maintain the same relationships between the zinc and the ferrocyanide.

Titration results are included in the tables. The end-point is sharp to within one drop. No indicator correction is necessary.

Titrations using 0·05M-*zinc solutions.*

0·05M-Zn taken (ml.).	0·025M-$K_4Fe(CN)_6$ added (ml.).	Back titrn. : 0·05M-Zn (ml.).	Total 0·05M-Zn consumed (ml.) : Found.	Calc.	0·05M-Zn taken (ml.).	0·025M-$K_4Fe(CN)_6$ added (ml.).	Back titrn. : 0·05M-Zn (ml.).	Total 0·05M-Zn consumed (ml.) : Found.	Calc.
25	40	4·98	29·98	30·00	15	25	3·74	18·74	18·75
25	40	5·00	30·00	30·00	10	15	1·24	11·24	11·25
20	30	2·52	22·52	22·50	10	15	1·25	11·25	11·25
20	30	2·49	22·49	22·50	5	7·50	0·60	5·60	5·63
15	25	3·7	18·72	18·75	5	7·50	0·63	5·63	5·63

Titrations using 0·005M-*zinc solutions.*

0·005M-Zn taken (ml.).	0·0025M-$K_4Fe(CN)_6$ added (ml.).	Back titrn. : 0·005M-Zn (ml.).	Total 0·005M-Zn consumed (ml.) : Found.	Calc.	0·005M-Zn taken (ml.).	0·0025M-$K_4Fe(CN)_6$ added (ml.).	Back titrn. : 0·005M-Zn (ml.).	Total 0·005M-Zn consumed (ml.) : Found.	Calc.
20	30	2·54	22·54	22·50	10	15	1·30	11·30	11·25
20	30	2·52	22·52	22·50	10	15	1·23	11·23	11·25
15	25	3·69	18·69	18·75	5	10	2·40	7·40	7·50
15	25	3·67	18·67	18·75	5	10	2·48	7·48	7·50

Titrations using 0·001M-*zinc solutions.*

0·001M-Zn taken (ml.).	0·0005M-$K_4Fe(CN)_6$ added (ml.).	Back titrn. : 0·001M-Zn (ml.).	Total 0·001M-Zn consumed (ml.) Found.	Calc.	0·001M-Zn taken (ml.).	0·0005M-$K_4Fe(CN)_6$ added (ml.).	Back titrn. : 0·001M-Zn (ml.).	Total 0·001M-Zn consumed (ml.) : Found.	Calc.
15	25	3·68	18·68	18·75	10	15	1·28	11·28	11·25
15	25	3·70	18·70	18·75	5	10	2·47	7·47	7·50
10	15	1·26	11·26	11·25	5	10	2·45	7·45	7·50

Experimental.

Solutions required.—Potassium ferrocyanide solution: 0·025, 0·0025, *and* 0·0005M. The 0·025M-solution was prepared by dissolving 10·551 g. of potassium ferrocyanide trihydrate and about 0·2 g. of sodium carbonate in water and diluting to one litre. The trihydrate was obtained by recrystallising

* Part VI, preceding paper.

pure potassium ferrocyanide and drying it to constant weight over a saturated solution of sodium chloride and sucrose. The weaker solutions were prepared from the stock 0·025M-solution by appropriate dilution.

Potassium ferricyanide solution: 1, 0·2, *and* 0·1%. Pure potassium ferricyanide was dissolved in water and kept in a dark bottle. The solution was prepared fresh daily.

Zinc sulphate solution: 0·05, 0·005, *and* 0·001M. The 0·05M-solution was prepared by dissolving 3·269 g. of pure zinc in a slight excess of dilute sulphuric acid and diluting to one litre with water. The weaker solutions were prepared by appropriate dilution of the stock 0·05M-solution. The concentration of this solution was checked by determining the zinc as the 8-hydroxyquinoline complex.

Indicator solution. 1 G. of 3 : 3′-dimethylnaphthidine was dissolved with warming in 100 ml. of glacial acetic acid.

Procedure.—Titrations using 0·05M-zinc solutions. The test solution containing zinc was treated with sufficient 2N-sulphuric acid to make its concentration about 1N. in a volume of 50 ml., and 10% ammonium sulphate solution was added to give a total concentration of 1 g. in 50 ml. Four drops of 1% potassium ferricyanide and two drops of indicator were added to this volume. A 10—20% excess of potassium ferrocyanide was run in rapidly with vigorous stirring. After a minute the solution became greyish-green and the excess of ferrocyanide was titrated with standard zinc solution to a change to purple-red.

Titrations using 0·005M-zinc solutions. The procedure described above was repeated except that the final concentration of sulphuric acid in 50 ml. was reduced to 0·2N., and that of ammonium sulphate to 0·4%. Four drops of 0·2% potassium ferricyanide solution and two drops of the indicator were added, and the titration carried out as above.

Titrations using 0·001M-zinc solutions. In this case the final concentration of sulphuric acid in 50 ml. was 0·1N., and that of ammonium sulphate was 0·2%. Four drops of 0·1% potassium ferricyanide and two drops of the indicator were added.

One of us (W. I. S.) is indebted to Messrs. Albright and Wilson Ltd. for a grant enabling him to carry out the work described in this and subsequent papers of this series.

CHEMISTRY DEPARTMENT,
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349. *Nitrosoacylarylamines. Part V.* The Nitrosation of 3-Acetamido-4-quinolones and -quinaldones.*

By (MRS.) W. J. ADAMS and D. H. HEY.

The alleged *O*-alkyl derivatives of substituted 4-hydroxyquinolines described by Colonna (*Gazzetta*, 1937, **67**, 46) are shown to be the corresponding *N*-alkyl derivatives. Whereas 3-amino-1-methyl-4-quinolone and its acetyl derivative are converted into 1-methyl-3-phenyl-4-quinolone by means of the triazen reaction or the nitrosoacetamido-derivative, respectively, the corresponding reactions with 3-amino-4-methoxyquinoline and its acetyl derivative fail. The nitrosation of 3-acetamido-1 : 2-dimethyl-4-quinolone gives a stable nitroso-derivative which is readily converted into 1-methylpyrazolo(4′ : 5′-2 : 3)-4-quinolone. 4-Hydroxy-3-phenylquinaldine is prepared by the cyclisation of ethyl β-anilino-α-phenylcrotonate.

THE preparation of 3-phenylquinoline from 3-aminoquinoline by the decomposition in benzene solution of 3-*N*-nitrosoacetamidoquinoline and of 3 : 3-dimethyl-1-3′-quinolyltriazen has been previously described (Adams, Hey, Mamalis, and Parker, *J.*, 1949, 3181). These reactions have now been applied to derivatives of 3-amino-4-hydroxy-quinoline and -quinaldine. A suitable series of 4-alkoxy-derivatives of 3-aminoquinoline appeared to have been prepared by Colonna (*Gazzetta*, 1937, **67**, 46), who obtained them by the action of methyl sulphate or alkyl iodides on 4-hydroxy-3-nitroquinoline followed by reduction.

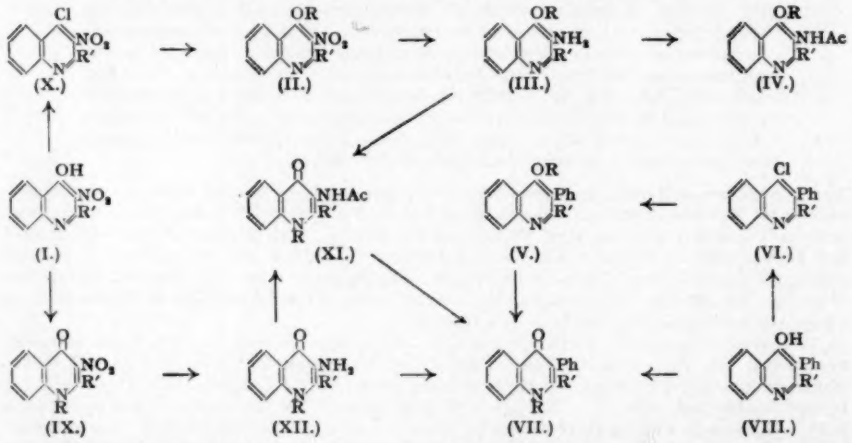
Treatment of 4-hydroxy-3-nitroquinoline (I; R′ = H) with methyl sulphate, as described by Colonna (*loc. cit.*), gave the alleged 4-methoxy-3-nitroquinoline (II; R = Me, R′ = H), which was converted by normal methods into the corresponding 3-amino- (III; R = Me, R′ = H) and 3-acetamido- (IV; R = Me, R′ = H) derivatives. The properties of these compounds were in agreement with those described by Colonna, although the melting point now recorded for the free base is the same as that recorded by Colonna for its hydrochloride, the constitution of which was not supported by analysis and which was reported to lose hydrogen chloride very

* Part IV, *J.*, 1940, 372.

readily. This alleged 3-amino-4-methoxyquinoline was then converted *via* the *N*-nitrosoacetamido-compound and the dimethyltriazen into a compound which gave a correct analysis for the expected 4-methoxy-3-phenylquinoline (V; R = Me, R′ = H) but which was not identical with 4-methoxy-3-phenylquinoline prepared by the action of sodium methoxide on 4-chloro-3-phenylquinoline (VI; R′ = H). The product was, however, identical with the isomeric 1-methyl-3-phenyl-4-quinolone (VII; R = Me, R′ = H) prepared by the action of methyl iodide and sodium methoxide on 4-hydroxy-3-phenylquinoline (VIII; R′ = H). The identity of the two isomeric methyl derivatives of 4-hydroxy-3-phenylquinoline was further confirmed by the conversion of 4-methoxy-3-phenylquinoline (V; R = Me, R′ = H) into 1-methyl-3-phenyl-4-quinolone (VII; R = Me, R′ = H) by heating its methiodide with 10% aqueous sodium hydroxide (cf. Knorr, *Ber.*, 1897, **30**, 922, 929; *Annalen*, 1903, **328**, 81).

This unexpected result necessitated a re-examination of the compounds described by Colonna (*loc. cit.*), since, unless some internal rearrangement had taken place in the course of his series of reactions, his starting materials must have been 1-alkyl-3-nitro-4-quinolones (IX; R′ = H) and not 4-alkoxy-3-nitroquinolines (II; R′ = H). It is known that, whereas alkylation of a 2- or 4-chloroquinoline with sodium alkoxides gives the *O*-alkyl derivative, alkylation of a 2- or 4-hydroxyquinoline with alkyl iodides (or with methyl sulphate) in the presence of alkali gives either an *O*- or an *N*-alkyl derivative, or a mixture of both, depending on experimental conditions and the presence of other substituents in the quinoline nucleus. It has been shown that, with 6- and 8-nitroquinoline and 5- and 8-nitroquinaldine, *O*-methyl derivatives are formed from the 4-chloro-compound, while *N*-methyl derivatives are obtained from the 4-hydroxy-compound (Halcrow and Kermack, *J.*, 1945, 415; Baker, Albisetti, Dodson, and Reigel, *J. Amer. Chem. Soc.*, 1946, **66**, 1532; Simpson and Wright, *J.*, 1948, 1707). In general, *O*-alkyl derivatives have lower melting points, are more soluble in organic solvents, and are less stable than the corresponding *N*-alkyl derivatives, into which they can in most cases be converted by heating, by treatment with alkali, or through the methiodides. The compounds prepared by Colonna could therefore have been either the *O*- or the *N*-alkyl derivatives but were assumed by him to be the former If his assumption is correct his compounds should be identical with the products obtained by the action of sodium alkoxides on 4-chloro-3-nitroquinoline.

4-Methoxy-3-nitroquinoline (II; R = Me, R′ = H), prepared by the action of sodium methoxide on 4-chloro-3-nitroquinoline (X; R′ = H), was not identical with the 4-methoxy-3-nitroquinoline described by Colonna (*loc. cit.*), and had a very much lower melting point and a greater solubility in alcohol. Attempts to prepare the corresponding amino-compound (III; R = Me, R′ = H) by reduction with stannous chloride and hydrochloric acid, as described by Colonna (*loc. cit.*) for his nitro-compound, were unsuccessful. 3-Amino-4-methoxyquinoline (III; R = Me, R′ = H) was, however, obtained by catalytic hydrogenation of the nitro-



compound, and was not identical with the amine described by Colonna (*loc. cit.*), to which this structure was assigned. Acetylation of this amine gave a compound which was identical with

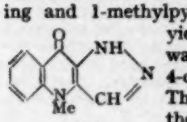
the acetyl derivative of the amine prepared as described by Colonna, and which had been shown to be the *N*-methylquinolone (XI; R = Me, R′ = H). This unexpected transformation to the quinonoid form during acetylation was confirmed when it was shown that acetylation under milder experimental conditions gave 3-acetamido-4-methoxyquinoline (IV; R = Me, R′ = H).

These investigations indicate that the methyl derivatives made by Colonna (*loc. cit.*) are actually 1-methyl-3-nitro-4-quinolone (IX; R = Me, R′ = H), 3-amino-1-methyl-4-quinolone (XII; R = Me, R′ = H), and 3-acetamido-1-methyl-4-quinolone (XI; R = Me, R′ = H), while those prepared in the course of the present work from 4-chloro-3-nitroquinolone are 4-methoxy-3-nitroquinoline (II; R = Me, R′ = H), 3-amino-4-methoxyquinoline (III; R = Me, R′ = H), and 3-acetamido-4-methoxyquinoline (IV; R = Me, R′ = H). Further, 4-ethoxy-3-nitroquinoline (II; R = Et, R′ = H), 3-nitro-4-*n*-propoxyquinoline (II; R = Pr^n, R′ = H), and 4-*n*-butoxy-3-nitroquinoline (II; R = Bu^n, R′ = H) were also prepared by the action of the corresponding sodium alkoxide on 4-chloro-3-nitroquinoline (X; R′ = H). These compounds were low-melting solids, different from those prepared by Colonna which must therefore be assumed to be the corresponding *N*-alkyl derivatives.

3-Amino-1-methyl-4-quinolone (XII; R = Me, R′ = H) was converted into 3 : 3-dimethyl-1-(1-methylquinol-4-on-3-yl)triazen and 1-methyl-3-*N*-nitrosoacetamido-4-quinolone was prepared by the action of nitrosyl chloride on 3-acetamido-1-methyl-4-quinolone (XI; R = Me, R′ = H). Decomposition of both these compounds in benzene solution gave 1-methyl-3-phenyl-4-quinolone (VII; R = Me, R′ = H), identified by comparison with an authentic specimen prepared by the action of methyl iodide on 4-hydroxy-3-phenylquinoline (VIII; R′ = H). Attempts to prepare similar derivatives of 3-amino-4-methoxyquinoline were unsuccessful. Treatment of 3-acetamido-4-methoxyquinoline (IV; R = Me, R′ = H) with nitrosyl chloride resulted in the recovery of unchanged starting material, and the product obtained by the reaction of diazotised 3-amino-4-methoxyquinoline (III; R = Me, R′ = H) with dimethylamine did not possess the properties of a triazen. It was therefore not possible to prepare 4-methoxy-3-phenylquinoline (V; R = Me, R′ = H) from 3-amino-4-methoxyquinoline (III; R = Me, R′ = H).

4-Hydroxy-3-nitroquinaldine (I; R′ = Me), prepared by the nitration of 4-hydroxyquinaldine by a modification of Halcrow and Kermack's method (*loc. cit.*), was converted in almost quantitative yield into 4-chloro-3-nitroquinaldine (X; R′ = Me) by gently warming it with phosphorus oxychloride (cf. Adams and Hey, *J.*, 1949, 3185). In preliminary work on the nitration of 4-hydroxyquinaldine an authentic specimen of the unknown 4-methoxy-6-nitroquinaldine became necessary; a preparation of this is described in the Experimental section. 4-Methoxy-3-nitroquinaldine (II; R = R′ = Me), 3-amino-4-methoxyquinaldine (III; R = R′ = Me), and 3-acetamido-4-methoxyquinaldine (IV; R = R′ = Me) were prepared from 4-chloro-3-nitroquinaldine (X; R′ = Me) as described for the corresponding compounds in the quinoline series. 4-Hydroxy-3-nitroquinaldine (I; R′ = Me) was recovered unchanged after being shaken for 18 hours with methyl sulphate in alkaline solution, but was alkylated by being heated with sodium methoxide and methyl iodide, and the 1 : 2-dimethyl-3-nitro-4-quinolone (IX; R = R′ = Me) was reduced and acetylated to give 3-amino-1 : 2-dimethyl-4-quinolone (XII; R = R′ = Me) and 3-acetamido-1 : 2-dimethyl-4-quinolone (XI; R = R′ = Me), as in the quinoline series.

The action of a solution of nitrosyl chloride in acetic anhydride on 3-acetamido-1 : 2-dimethyl-4-quinolone (XI; R = R′ = Me) gave 1 : 2-dimethyl-3-*N*-nitrosoacetamido-4-quinolone as a pale yellow powder, decomposing, without melting, at 131°, which was found to be unusually stable and could be exposed to the air for several weeks without undergoing decomposition. When a solution of this nitroso-compound in benzene was boiled under reflux there was no darkening and 1-methylpyrazolo(4′ : 5′-2 : 3)-4-quinolone (XIII) separated in almost quantitative yield from the hot solution as a yellow crystalline solid. This compound was also formed during the prolonged nitrosation of 3-acetamido-1 : 2-dimethyl-4-quinolone, thus confirming the non-participation of benzene in the reaction. The formation of this compound by cyclisation involving the nitroso-group and the *o*-methyl group is not unexpected. It is well-known that indazoles are obtained from diazotised *o*-toluidines and from *N*-nitrosoacyl-*o*-toluidines and the known reactivity of the 2-methyl group in the pyridine and quinoline series must render this type of reaction in the heterocyclic series extremely facile.



(XIII.)

The action of nitrosyl chloride on 3-acetamido-4-methoxyquinaldine (IV; R = R′ = Me) gave a yellow oil which did not appear to act normally. The abnormal behaviour of both 3-acetamido-4-methoxy-quinoline and -quinaldine in these reactions is unexpected. That such

behaviour is not entirely due to the *o*-methoxyl group in these benzenoid structures is indicated by the fact that *o*-anisidine reacts normally (as the diazonium salt) with pyridine to give a mixture of *o*-methoxyphenylpyridines in 50% yield (Haworth, Heilbron, and Hey, *J.*, 1940, 358), although in a reaction with 1-*o*-methoxyphenyl-3 : 3-dimethyltriazen and benzene 2-methoxydiphenyl was isolated in only 10% yield.

Although 4-hydroxy-3-phenylquinaldine derivatives could not be obtained by the reaction of derivatives of 3-aminoquinaldine with benzene, 4-hydroxy-3-phenylquinaldine itself (VIII; R′ = Me) was made available in small yield by the ring closure in boiling phenyl ether of ethyl β-anilino-α-phenylcrotonate, obtained by the condensation of ethyl α-phenylacetoacetate with aniline.

Experimental.

1-*Methyl*-3-*nitro*-4-*quinolone* (cf. Colonna, *loc. cit.*).—4-Hydroxy-3-nitroquinoline (Bachmann, Welton, Jenkins, and Christian, *J. Amer. Chem. Soc.*, 1947, **69**, 365) (5 g.) was dissolved in a solution of potassium hydroxide (2 g.) in water (50 c.c.), and methyl sulphate (3·3 g.) was added. The mixture was shaken for 20 minutes and left at room temperature overnight. The precipitated yellow solid was filtered off, washed with aqueous potassium hydroxide and with water, and dried. 1-Methyl-3-nitro-4-quinolone (4·5 g.) was obtained in pale straw-coloured needles, m. p. 219·5—220·5°, after recrystallisation from alcohol. Colonna (*loc. cit.*) who describes this compound as 4-methoxy-3-nitroquinoline, gives m. p. 220°. Since the completion of this work, Price (*Australian J. Sci. Res.*, 1949, *A*, **2**, 272) has reported the preparation of 1-methyl-3-nitro-4-quinolone by the nitration of 1-methyl-4-quinolone. He records m. p. 227—229° (corr.).

3-*Amino*-1-*methyl*-4-*quinolone* (cf. Colonna, *loc. cit.*).—A hot solution of stannous chloride (50 g.) in concentrated hydrochloric acid (50 c.c.) was added with stirring to a suspension of 1-methyl-3-nitro-4-quinolone (10 g.) in glacial acetic acid (100 c.c.). There was an immediate vigorous reaction. The mixture was heated on the water-bath for 1 hour, then left overnight at room temperature. The filtered product was heated with 50% aqueous sodium hydroxide for 10 minutes. The resulting yellow solid was filtered off and washed quickly with cold water. 3-Amino-1-methyl-4-quinolone (8·7 g.) was obtained in yellow needles, m. p. 153—156°, by recrystallisation from benzene or toluene. Colonna (*loc. cit.*) gives m. p. 155° for this compound, which he describes as the hydrochloride of 3-amino-4-methoxyquinoline. Price (*loc. cit.*) records m. p. 234—235° (decomp.) for the picrate of this base.

3-*Acetamido*-1-*methyl*-4-*quinolone* (cf. Colonna, *loc. cit.*).—3-Amino-1-methyl-4-quinolone (8 g.) was boiled under reflux with acetic anhydride (25 c.c.) for 1 hour. The solution was poured into water (100 c.c.) and made alkaline with aqueous sodium hydroxide. Recrystallisation of the precipitated solid from water gave 3-acetamido-1-methyl-4-quinolone (8·4 g.) in white needles, m. p. 214—216°. Colonna, who describes this compound as 3-acetamido-4-methoxyquinoline, gives m. p. 216°.

4-*Methoxy*-3-*nitroquinoline*.—A methanolic solution of 4-chloro-3-nitroquinoline (Albert, Brown, and Duewell, *J.*, 1948, 1288) (3 g.) and sodium methoxide [from sodium (0·33 g.) and methyl alcohol (50 c.c.)] was boiled under reflux for 1 hour, and poured into water (200 c.c.). The solid product was filtered off, washed with water, and dried at 60°. 4-*Methoxy*-3-*nitroquinoline* (2·8 g.) separated from light petroleum (b. p. 40—60°) in long yellow needles, m. p. 99—100° (Found : C, 59·1; H, 4·0. $C_{10}H_8O_3N_2$ requires C, 58·8; H, 3·9%).

3-*Amino*-4-*methoxyquinoline*.—A suspension of 4-methoxy-3-nitroquinoline (3 g.) in methyl alcohol (15 c.c.) was shaken with hydrogen at atmospheric pressure and room temperature in the presence of platinum. When hydrogen uptake (3 moles) ceased, the solution was filtered and the solvent removed under reduced pressure. Crystallisation of the residue gave 3-*amino*-4-*methoxyquinoline monohydrate* (2·4 g.) in brown transparent plates from benzene, or pinkish needles from water. Both forms had m. p. 75—80°, raised to 81° after being dried over phosphoric oxide *in vacuo* for 3 weeks (Found, for specimen dried at 80° at atmospheric pressure : C, 63·2; H, 6·3. $C_{10}H_{10}ON_2,H_2O$ requires C, 62·6; H, 6·3%).

Action of Acetic Anhydride on 3-*Amino*-4-*methoxyquinoline*.—(i) 3-Amino-4-methoxyquinoline (0·5 g.) was heated under reflux with acetic anhydride (5 c.c.) for 1 hour. After removal of half of the excess of solvent by distillation the remaining solution was poured into water (20 c.c.). Addition of aqueous sodium hydroxide precipitated 3-acetamido-1-methyl-4-quinolone as a white solid which crystallised from water in white needles, m. p. 213—214° undepressed on admixture with an authentic specimen prepared as described above.

(ii) Sulphuric acid (3 drops) was added to a mixture of 3-amino-4-methoxyquinoline (0·81 g.) and acetic anhydride (2 c.c.). After 1 hour at room temperature the solution was diluted with water (5 c.c.) and made alkaline with aqueous sodium hydroxide. The precipitated 3-*acetamido*-4-*methoxyquinoline hemihydrate* crystallised from water in white needles (0·77 g.), m. p. 74° after being dried below 50°, raised to 97—101° after being dried for 3 weeks over potassium hydroxide *in vacuo*, and to 105° after being dried for 3 hours over potassium hydroxide *in vacuo* at 100° (Found, for specimen, m. p. 105° : C, 65·9; H, 5·4; N, 13·1. $C_{12}H_{12}O_2N_2$ requires C, 66·7; H, 5·5; N, 13·0%. Found, for specimen, m. p. 74° : C, 64·5; H, 5·8. $C_{12}H_{12}O_2N_2,\frac{1}{2}H_2O$ requires C, 64·0; H, 5·8%).

4-*Ethoxy*-3-*nitroquinoline*.—A mixture of 4-chloro-3-nitroquinoline (2·3 g.) and sodium ethoxide [from sodium (0·26 g.) in dry ethyl alcohol (25 c.c.)] was boiled under reflux for 3 hours. The solution was diluted and the precipitated solid filtered off and dried. 4-*Ethoxy*-3-*nitroquinoline* (1·9 g.) separated from aqueous methyl alcohol or light petroleum in straw-coloured plates, m. p. 57·5° (Found : C, 60·4; H, 4·6. $C_{11}H_{10}O_3N_2$ requires C, 60·5; H, 4·6%). Colonna (*loc. cit.*) gave m. p. 202° for the compound to which this structure was assigned, but which must now be regarded as 1-ethyl-3-nitro-4-quinolone.

3-*Nitro*-4-n-*propoxyquinoline*.—A mixture of 4-chloro-3-nitroquinoline (3·5 g.) and sodium propoxide

[from sodium (0·4 g.) in dry *n*-propyl alcohol (40 c.c.)] was boiled under reflux for 3 hours. After dilution with water, the oil which separated was extracted with ether. The dried (Na_2SO_4) ethereal solution was evaporated and the residue was extracted with light petroleum (b. p. 40—60°). The insoluble residue, after crystallisation from methyl alcohol, had m. p. 119—120° and consisted of unchanged 4-chloro-3-nitroquinoline. Concentration of the light petroleum extract gave 3-*nitro*-4-n-*propoxyquinoline* in pale yellow prisms (2·6 g.), m. p. 42—43° (Found: C, 61·8; H, 5·2. $C_{12}H_{12}O_3N_2$ requires C, 62·1; H, 5·2%). Colonna (*loc. cit.*) gave m. p. 156° for the compound to which this structure was assigned, but which must now be regarded as 3-nitro-1-*n*-propyl-4-quinolone.

4-n-*Butoxy*-3-*nitroquinoline*.—4-Chloro-3-nitroquinoline (2 g.) was added to a solution of sodium butoxide [from sodium (0·22 g.) in *n*-butyl alcohol (25 c.c.)], and the solution was boiled under reflux for 3 hours. The solid obtained on dilution with water was filtered off and dried. 4-n-*Butoxy*-3-*nitroquinoline* separated from light petroleum (b. p. 40—60°) in yellow transparent plates (1·7 g.), m. p. 53—54° (Found: C, 64·1; H, 6·0. $C_{13}H_{14}O_3N_2$ requires C, 63·4; H, 5·7%). Colonna, *loc. cit.*, gave m. p. 140° for the compound to which this structure was assigned, but which must now be regarded as 1-*n*-butyl-3-nitro-4-quinolone.

1-*Methyl*-3-*phenyl*-4-*quinolone*.—(i) *From* 4-*hydroxy*-3-*phenylquinoline*. Methyl iodide (5 c.c.) was added to a methanolic solution of 4-hydroxy-3-phenylquinoline (0·7 g.) and sodium methoxide [from sodium (0·2 g.) in dry methyl alcohol (15 c.c.)]. The solution was boiled under reflux for 4 hours, and then concentrated and diluted with water (20 c.c.). The precipitated solid was filtered off and dried. 1-*Methyl*-3-*phenyl*-4-*quinolone hemihydrate* was obtained in white needles, m. p. 125—126°, after recrystallisation from aqueous methyl alcohol (Found: C, 78·8; H, 5·6. $C_{16}H_{13}ON,\frac{1}{2}H_2O$ requires C, 78·7; H, 5·7%). It was insoluble in ether and light petroleum, but soluble in hot ethyl alcohol. The *picrate*, long yellow needles from ethyl alcohol, had m. p. 150—151° (Found: C, 56·9; H, 3·9. $C_{16}H_{13}ON,C_6H_3O_7N_3$ requires C, 56·9; H, 3·5%). The methiodide was prepared by heating a methyl alcoholic solution of the base with methyl iodide, followed by concentration and precipitation with ether. It separated in cream-yellow micro-needles, m. p. 156·5—161·5°, but attempted recrystallisation caused decomposition.

(ii) *From* 3 : 3-*dimethyl*-1-(1-*methylquinol*-4-*on*-3-*yl*)*triazen* (cf. Elks and Hey, *J.*, 1943, 441). 3-Amino-1-methyl-4-quinolone (7·2 g.) was dissolved in a mixture of concentrated hydrochloric acid (9·9 c.c.) and water (60 c.c.), and the resulting suspension of hydrochloride stirred vigorously at 0—5° while a solution of sodium nitrite (3·2 g.) in water (20 c.c.) was added slowly. Stirring was continued for 15 minutes after completion of addition. The resulting solution was added to a cooled, stirred mixture of 33% aqueous dimethylamine (6·7 g.) and a solution of anhydrous sodium carbonate (7·6 g.) in water (80 c.c.). After 30 minutes the precipitated 3 : 3-dimethyl-1-(1-methylquinol-4-on-3-yl)triazen was filtered off, washed with water, and dried *in vacuo*. Repeated recrystallisation from benzene gave the triazen as a fawn, crystalline solid, m. p. varying between 100° and 109° with decomposition. An analytically pure specimen could not be obtained. Dry hydrogen chloride was passed through a solution of the triazen (6 g.) in dry benzene (250 c.c.), heated under reflux on a water-bath for 5 hours. The solution was washed with 10% aqueous sodium hydroxide and decanted from the tar. The dried (Na_2SO_4) benzene layer was concentrated by evaporation under reduced pressure. From the residual red oil, by repeated recrystallisation from ethyl alcohol, 1-methyl-3-phenyl-4-quinolone was obtained in white needles, m. p. 118·5—120·5° undepressed on admixture with a specimen prepared as described above. The picrate had m. p. 152°, undepressed on admixture with 1-methyl-3-phenyl-4-quinolone picrate described above.

(iii) *From* 1-*methyl*-3-N-*nitrosoacetamido*-4-*quinolone* (cf. France, Heilbron, and Hey, *J.*, 1940, 369). A 20% solution of nitrosyl chloride in acetic acid (13 c.c.) was added slowly to a stirred mixture of 3-acetamido-1-methyl-4-quinolone (3·8 g.), acetic anhydride (10 c.c.), acetic acid (15 c.c.), phosphoric oxide (0·5 g.), and fused potassium acetate (6 g.), cooled to 0—5°, and stirring was continued for 20 minutes after addition. The yellow solution was poured on crushed ice, and sufficient solid sodium carbonate was added to make the solution alkaline. 1-Methyl-3-*N*-nitrosoacetamido-4-quinolone separated as a brown oil, which gradually solidified. It was filtered off, washed with ice-cold water, dried *in vacuo* (m. p. 50—52° with decomp.), and then added to dry benzene (300 c.c.), which solution was decanted from a small amount of insoluble residue. The solution was maintained at 60° for 7 hours; evolution of nitrogen started at about 40°. Removal of the solvent left a dark-red oil, from which, by recrystallisation from aqueous ethyl alcohol, 1-methyl-3-phenyl-4-quinolone, m. p. 125—126°, was obtained (Found: C, 78·4; H, 5·8. $C_{16}H_{13}ON,\frac{1}{2}H_2O$ requires C, 78·7; H, 5·7%). The picrate separated in bright yellow needles, m. p. 152°, from ethyl alcohol. The melting points of the free base and the picrate were not depressed on admixture with the compounds prepared by methods (i) and (ii) above.

4-*Methoxy*-3-*phenylquinoline*.—4-Chloro-3-phenylquinoline (1 g.) was added to a solution of sodium methoxide [from sodium (0·2 g.) in dry methyl alcohol (10 c.c.)], and the solution was boiled under reflux for 2 hours. The mixture was poured into ice water and the solid which gradually separated was filtered off. 4-*Methoxy*-3-*phenylquinoline* (0·7 g.) crystallised from light petroleum (b. p. 40—60°) in stout prisms, m. p. 82—83° (Found: C, 81·5; H, 5·7. $C_{16}H_{13}ON$ requires C, 81·7; H, 5·3%). It was soluble in cold ether and in ethyl alcohol. The *picrate*, shining yellow micro-needles from ethyl alcohol, had m. p. 157·5—159·5° (Found: C, 56·1, H, 3·3. $C_{16}H_{13}ON,C_6H_3O_7N_3$ requires C, 56·9; H, 3·5%). The methiodide, orange yellow micro-needles, m. p. 151—153°, was prepared by heating a methyl-alcoholic solution of the base with methyl iodide for 5 hours, followed by concentration and precipitation with ether. Attempted recrystallisation caused decomposition. By boiling the methiodide for 1 hour with 10% aqueous sodium hydroxide, 1-methyl-3-phenyl-4-quinolone was obtained, identified by melting point and mixed melting point.

Nitration of 4-*Hydroxyquinaldine* (cf. Halcrow and Kermack, *loc. cit.*).—A mixture of 4-hydroxyquinaldine (33 g.) and concentrated nitric acid (330 c.c.) was heated at 100° for 1 hour. The resultant orange solution was poured into ice and water (1500 c.c.). The precipitated yellow solid was filtered

off, suspended in water, filtered off again, thoroughly washed with water, and dried (25 g.). Extraction of this product with boiling water (2 × 500 c.c.) left 4-hydroxy-3-nitroquinaldine (21·6 g.) as a light yellow powder, m. p. >360°.

1 : 2-*Dimethyl*-3-*nitro*-4-*quinolone*.—A solution of 4-hydroxy-3-nitroquinaldine (6·5 g.) in methyl alcohol (60 c.c.) containing sodium methoxide [from sodium (2 g.)] was heated with methyl iodide (10 c.c.) for 16 hours. More methyl iodide (10 c.c.) was added and heating was continued for a further 8 hours. Excess of solvent was removed and the residue was treated with water (200 c.c.). The precipitated brown solid was filtered off, washed, and dried. 1 : 2-*Dimethyl*-3-*nitro*-4-*quinolone* (3·7 g.) crystallised from ethyl alcohol in pale yellow shining leaflets, m. p. 227—228° (Found : C, 60·3; H, 4·8. $C_{11}H_{10}O_3N_2$ requires C, 60·5; H, 4·6%).

3-*Amino*-1 : 2-*dimethyl*-4-*quinolone*.—A hot solution of stannous chloride (15 g.) in concentrated hydrochloric acid (15 c.c.) was added with stirring to a hot solution of 1 : 2-dimethyl-3-nitro-4-quinolone (2·9 g.) in glacial acetic acid (30 c.c.). There was an immediate vigorous reaction, and after being left at room temperature overnight the precipitated stannichloride was filtered off, washed, and boiled for 15 minutes with 50% aqueous sodium hydroxide (50 c.c.). The solid so obtained was crystallised from hot water. 3-*Amino*-1 : 2-*dimethyl*-4-*quinolone* (2·2 g.) separated in pale yellow needles, m. p. 180·5—181° (Found : C, 69·4; H, 6·5. $C_{11}H_{12}ON_2$ requires C, 70·2; H, 6·4%). Acetylation of 3-amino-1 : 2-dimethyl-4-quinolone (1·9 g.) with acetic anhydride gave 3-*acetamido*-1 : 2-*dimethyl*-4-*quinolone* (1·6 g.) in small white needles, m. p. 255—257°, from water (Found : C, 67·4; H, 6·0. $C_{13}H_{14}O_2N_2$ requires C, 67·8; H, 6·1%).

4-*Chloro*-3-*nitroquinaldine*.—4-Hydroxy-3-nitroquinaldine (10 g.) was heated gently with phosphorus oxychloride (100 c.c.) until the solid had just dissolved (10 minutes). The resulting solution was added very slowly to a mixture of ammonia solution and crushed ice, so that the solution remained alkaline to phenolphthalein. The precipitated solid was filtered off, washed with dilute ammonia solution and water, and dried *in vacuo* (KOH). 4-Chloro-3-nitroquinaldine (9·8 g., 90%) was obtained as a pale brown, crystalline solid, m. p. 90—93°, after recrystallisation from benzene. Conrad and Limpach (*Ber.*, 1888, **21**, 1981) give m. p. 93—94° for 4-chloro-3-nitroquinaldine prepared from 4-hydroxy-3-nitroquinaldine in only 45% yield.

4-*Methoxy*-3-*nitroquinaldine*.—A solution of 4-chloro-3-nitroquinaldine (9·7 g.) in methyl alcohol (50 c.c.) containing sodium methoxide [from sodium (1 g.)], was heated for 2 hours. Dilution with water precipitated a solid which was filtered off, washed with water, and dried at 50°. 4-*Methoxy*-3-*nitroquinaldine* (6·9 g.) separated from light petroleum (b. p. 40—60°) in deep cream crystals, m. p. 79·5—81° (Found : C, 60·6; H, 4·5. $C_{11}H_{10}O_3N_2$ requires C, 60·5; H, 4·6%).

3-*Amino*-4-*methoxyquinaldine*.—A suspension of 4-methoxy-3-nitroquinaldine (5 g.) in ethyl alcohol containing platinum was shaken with hydrogen at room temperature and atmospheric pressure. When the theoretical quantity of hydrogen had been absorbed the solution was filtered and evaporated. The solid residue was dissolved in hot water and filtered from an insoluble oil. 3-*Amino*-4-*methoxyquinaldine* (3·4 g.) crystallised from the cooled solution in cream needles, m. p. 112—113° (Found : C, 70·2; H, 6·4. $C_{11}H_{12}ON_2$ requires C, 70·2; H, 6·4%). Concentrated sulphuric acid (1 drop) was added to 3-amino-4-methoxyquinaldine (3·3 g.) in acetic anhydride (10 c.c.). After 2 hours at room temperature the solution was diluted with water and made alkaline with aqueous sodium hydroxide, which precipitated a gelatinous mass which became solid on storage. 3-*Acetamido*-4-*methoxyquinaldine* (2·5 g.) separated from water in clusters of white silky needles, m. p. 189° (Found : C, 67·5; H, 6·2. $C_{13}H_{14}O_2N_2$ requires C, 67·8; H, 6·1%).

Action of Nitrosyl Chloride on 3-*Acetamido*-1 : 2-*dimethyl*-4-*quinolone*.—A 25% solution of nitrosyl chloride in acetic anhydride (8 c.c.) was added slowly to a solution of 3-acetamido-1 : 2-dimethyl-4-quinolone (1·86 g.) in acetic acid (17 c.c.) and acetic anhydride (5 c.c.) containing fused potassium acetate (5 g.) and phosphoric oxide (0·3 g.), stirred at 0—5°. Stirring was continued for 1 hour after the addition was complete, and the resulting solution was poured on crushed ice (50 g.) and made alkaline with aqueous sodium carbonate. The 1 : 2-dimethyl-3-*N*-nitrosoacetamido-4-quinolone (1·5 g.) which separated as a pale yellow powder was filtered off, washed with water, and dried (KOH) *in vacuo*. It decomposed to a brown solid on being heated to 131°, and decomposed with a flash when placed in a flame. 1 : 2-Dimethyl 3-*N*-nitrosoacetamido-4-quinolone (0·5 g.) was dissolved in warm benzene (100 c.c.), and the solution was boiled under reflux for 2 hours. A yellow solid (0·3 g.) separated from the hot solution, and more (0·08 g.) was obtained by evaporation of the benzene solution. 1-*Methylpyrazolo*(4′ : 5′-2 : 3)-4-*quinolone* separated from ethyl alcohol in yellow-fawn micro-needles, m. p. 340—342° (some decomp. >325°) (Found : C, 66·4; H, 4·3; N, 20·9. $C_{11}H_9ON_3$ requires C, 66·4; H, 4·5; N, 21·1%). It was practically insoluble in benzene, only slightly soluble in alcohol, and slightly soluble in hot water, from which solution it separated in pale yellow needles on cooling. Solutions showed an intense violet fluorescence.

4-*Methoxy*-6-*nitroquinaldine*.—4-Chloro-6-nitroquinaldine (0·21 g.) (Kermack and Weatherhead, *J.*, 1939, 566) was added to a solution of sodium methoxide [from sodium (0·02 g.) in dry methyl alcohol (10 c.c.)] and the whole heated under reflux for 2 hours. The solution was diluted with water (30 c.c.), and the precipitated solid was filtered off, washed, and dried. 4-*Methoxy*-6-*nitroquinaldine* was insoluble in light petroleum (b. p. 40—60°) and crystallised from ethyl alcohol in pale fawn needles, m. p. 192—193° (Found : C, 60·2; H, 4·6. $C_{11}H_{10}O_3N_2$ requires C, 60·5; H, 4·6%).

1-o-*Methoxyphenyl*-3 : 3-*dimethyltriazen* (cf. Elks and Hey, *loc. cit.*).—A solution of *o*-methoxybenzenediazonium chloride, prepared by the slow addition of a solution of sodium nitrite (7·6 g.) in water (50 c.c.) to a solution of *o*-anisidine (12·3 g.) in concentrated hydrochloric acid (24 c.c.) and water (100 c.c.) stirred at 0—5°, was added slowly, with stirring, to a cooled mixture of 33% aqueous dimethylamine (16 g.) and sodium carbonate (18 g.) in water (150 c.c.). The dark red oil which separated was extracted with ether and dried (Na_2SO_4). The residue after removal of solvent was distilled under reduced pressure. 1-o-*Methoxyphenyl*-3 : 3-*dimethyltriazen* (16 g.) was collected at 123—124°/8 mm., or 155°/18 mm. as a pale yellow oil (Found : C, 60·8; H, 7·7. $C_9H_{13}ON_3$ requires C, 60·3; H, 7·3%).

2-Methoxydiphenyl.—A solution of 1-*o*-methoxyphenyl-3 : 3-dimethyltriazen (5 g.) in dry benzene (50 c.c.) was heated on a water-bath while a slow stream of dry hydrogen chloride was passed through it. After 1 hour the reaction mixture was cooled, the precipitated solid was filtered off, and the benzene solution was washed with 10% aqueous sodium hydroxide. Evaporation of the dried ($MgSO_4$) benzene solution left a red oil, which was distilled under reduced pressure. 2-Methoxydiphenyl (0·5 g.) was obtained as a slightly yellow, viscous oil, b. p. 124—128°/3—4 mm. [Borsche and Scholten (*Ber.*, 1917, **50**, 601), give b. p. 159—160°/18 mm.; von Auwers and Harres (*Z. physikal. Chem.*, *A*, 1929, **143**, 14) give b. p. 150°/13 mm.]. Nitration of 2-methoxydiphenyl as described by Borsche and Scholten (*loc. cit.*) gave 2-methoxy-5-nitrodiphenyl, which separated from methyl alcohol in pale yellow needles, m. p. 94—95° (Borsche and Scholten, *loc. cit.*, give m. p. 95—96°).

4-Hydroxy-3-phenylquinaldine.—Ethyl α-phenylacetoacetate was prepared by the hydrolysis of α-phenylacetoacetonitrile as described in *Org. Synth.*, Coll. Vol. II, 1943, 284. The crude ester (42 g.), containing some unchanged nitrile which proved difficult to separate, was added to aniline (20 g.) together with concentrated hydrochloric acid (3 drops). After 24 hours at room temperature the water formed was removed and the dried ($MgSO_4$) oil was added to boiling phenyl ether (250 c.c.), and the solution heated for 1½ hours. The solid which separated on cooling was filtered off, washed thoroughly with light petroleum (b. p. 40—60°), and dried. Recrystallisation from ethyl alcohol gave *4-hydroxy-3-phenylquinaldine* (1·87 g.) in cream needles, m. p. 302—304° (decomp.) (Found: C, 82·2; H, 5·7. $C_{16}H_{13}ON$ requires C, 81·7; H, 5·5%).

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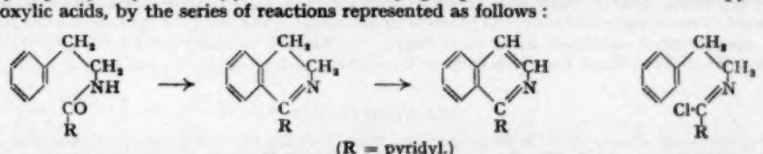
350. 1-*Pyridylisoquinolines.*

By D. H. HEY and J. M. WILLIAMS.

Several 1-3′- and 1-4′-pyridyl*iso*quinolines have been prepared by the application of the Bischler–Napieralski reaction, or modifications thereof, to the appropriate nicotin- or *iso*nicotin-amides, followed by dehydrogenation. Observations have been made on the facility of the cyclisation and dehydrogenation stages in the synthesis of the compounds studied. An abortive attempt to obtain a pyridyl*iso*quinoline, in which the pyridyl group is attached to the carbocyclic nucleus, is described.

THE long-known spasmolytic action of papaverine, coupled with the recently discovered antispasmodic activity in certain pyridylquinolines (Coates, Cook, Heilbron, Hey, Lambert, and Lewis, *J.*, 1943, 401 and subsequent papers), suggested that members of the pyridyl*iso*quinoline series might be worthy of study. The significance of this suggestion was emphasised by the claim that 3-methyl-6 : 7-methylenedioxy-1-3′-pyridyl*iso*quinoline had in fact been prepared and was described as an excellent substitute for papaverine (Merck, D.R.-P. 549,967). No further members of this series, however, appear to have been prepared, although it has been reported that the synthesis of the closely related 6 : 7-methylenedioxy-1-2′-picolyl*iso*quinoline has been attempted (Clemo, McIlwain, and Morgan, *J.*, 1936, 610; Bills and Noller, *J. Amer. Chem. Soc.*, 1948, **70**, 957) but failed because the corresponding 3 : 4-dihydro*iso*quinoline could not be dehydrogenated. The preparation of 3 : 4-dihydro-6 : 7-dimethoxy-1-3′-pyridyl*iso*quinoline has been reported by Sugusawa and Kuriyagawa (*Ber.*, 1936, **69**, 2068) and it would appear that attempts to dehydrogenate this compound were also unsuccessful.

By means of the Bischler–Napieralski reaction (*Ber.*, 1893, **26**, 1903), or modifications thereof (*e.g.*, Decker and Kropp, *Ber.*, 1909, **42**, 2075; Decker, Kropp, Hoyer, and Becker, *Annalen*, 1913, **395**, 299), a series of 1-pyridyl*iso*quinolines (III) should result from the ring closure of *N*-acyl-2-phenylethylamines (I), in which the acyl group is derived from one of the pyridinecarboxylic acids, by the series of reactions represented as follows:



(I.) (II.) (III.) (IV.)

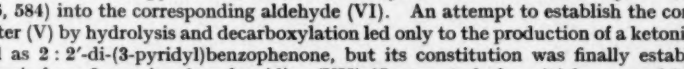
It was found, however, that neither *N*-nicotinoyl-2-phenylethylamine nor *N-iso*nicotinoyl-2-phenylethylamine could be converted into the dihydro*iso*quinoline (II) by the action of phos-

phoric oxide or phosphorus oxychloride in boiling toluene or xylene, but when decalin was used as solvent the formation of the dihydro*iso*quinolines took place in low yield with much simultaneous decomposition. Excellent yields of the dihydro*iso*quinolines were obtained when the modified procedure due to Decker and Kropp (*loc. cit.*) was used. In this method the imidochloride (IV), formed by the action of phosphorus pentachloride on the acyl-2-phenylethylamine, is treated with aluminium chloride. In addition to 3 : 4-dihydro-1-3′- and -1-4′-pyridyl*iso*quinoline, the 3- and 4-methyl derivatives of each of these were prepared in this manner with the use of 1-phenyl-2-propylamine or 2-phenyl-*n*-propylamine in place of 2-phenylethylamine. The six dihydro*iso*quinolines were dehydrogenated by heating them with palladium–charcoal to give the corresponding *iso*quinolines.

N-Nicotinoyl- and *N-iso*nicotinoyl-2-(3 : 4-methylenedioxyphenyl)ethylamine were converted into the corresponding 3 : 4-dihydro-1-pyridyl*iso*quinolines in the normal manner by the action of phosphorus pentachloride in boiling xylene, the reaction being facilitated in these compounds by the strong activating influence of the methylenedioxy-group. The resulting compounds have been assigned the structures of 3 : 4-dihydro-6 : 7-methylenedioxy-1-3′- and -1-4′-pyridyl-*iso*quinoline by analogy with the formation of 3 : 4-dihydro-6 : 7-methylenedioxy-1-phenyl*iso*-quinoline from benzoyl-2-(3 : 4-methylenedioxyphenyl)ethylamine as described by Decker Kropp, Hoyer, and Becker (*loc. cit.*). On the other hand, *N*-nicotinoyl- and *N-iso*nicotinoyl-2-*p*-chlorophenylethylamine required conversion to the imidochloride and subsequent treatment with aluminium chloride in order to obtain the corresponding dihydro*iso*quinolines. The attempted dehydrogenation of these four substituted 3 : 4-dihydro*iso*quinolines by heating them with palladium–charcoal led to complete disintegration, but it was found possible to convert 3 : 4-dihydro-6 : 7-methylenedioxy-1-3′-pyridyl*iso*quinoline into 6 : 7-methylenedioxy-1-3′-pyridyl*iso*quinoline by the action of bromine in dioxan solution.

Harwood and Johnstone (*J. Amer. Chem. Soc.*, 1934, **56**, 468) have reported the facile dehydrogenation of 3 : 4-dihydro-6 : 7-dimethoxy-1-phenyl*iso*quinoline-3-carboxylic acid by the action of thionyl chloride, and the presence of a group in the 3-position may account for the successful preparation of 3-methyl-6 : 7-methylenedioxy-1-3′-pyridyl*iso*quinoline as reported in D.R.-P. 549,967. The failures at the dehydrogenation stage reported above, together with similar observations recorded elsewhere (Clemo, McIlwain, and Morgan, and Bills and Noller, *locc. cit.*), led to a repetition of the synthesis of 3-methyl-6 : 7-methylenedioxy-1-3′-pyridyl*iso*-quinoline. Apart from discrepancies in the physical constants of the intermediate compounds the synthesis has been confirmed and both the dihydro*iso*quinoline and the *iso*quinoline have been further characterised as the picrates.

In an attempt to obtain an *iso*quinoline derivative with a pyridyl group attached to the carbocyclic ring, attention was directed to the possibility of the cyclisation of the amino-acetals of suitable pyridylbenzaldehydes following the general procedure of Pomeranz (*Monatsh.*, 1893, **14**, 116; 1894, **15**, 299). Methyl *o*-3-pyridylbenzoate (V), prepared by the action of diazotised



(R = 3-pyridyl.)

(VII.) (VIII.) (V.) (VI.)

methyl anthranilate on pyridine, was converted by the method of McFadyen and Stevens (*J.*, 1936, 584) into the corresponding aldehyde (VI). An attempt to establish the constitution of the ester (V) by hydrolysis and decarboxylation led only to the production of a ketonic product regarded as 2 : 2′-di-(3-pyridyl)benzophenone, but its constitution was finally established by its synthesis from 3-*o*-aminophenylpyridine (VII) (Coates *et al.*, *loc. cit.*) by way of 3-2′-cyano-phenylpyridine (VIII) and *o*-3-pyridylbenzoic acid. *o*-3-Pyridylbenzylideneaminoacetal, prepared from *o*-3-pyridylbenzaldehyde and aminoacetal, could not be cyclised by treatment with concentrated sulphuric acid, phosphorus oxychloride, or anhydrous hydrogen fluoride. Similar attempts to effect the cyclisation of 4-phenylbenzylideneaminoacetal were also abortive.

Experimental.

Preparation of Bases.—2-(3 : 4-Methylenedioxyphenyl)ethylamine was prepared by the method of Decker *et al.* (*Annalen*, 1913, **395**, 291), and 2-*p*-methoxyphenylethylamine by the method of Barger and Walpole (*J.*, 1909, **95**, 1724).

2-*Phenyl*-n-*propylamine*. To β-phenyl-*n*-butyric acid (27 g.) at room temperature an excess of thionyl chloride was added, and after the vigorous reaction had subsided the mixture was heated for a

further 2 hours at 60°. The excess of thionyl chloride was then removed under reduced pressure and the residual oil kept overnight in a desiccator (KOH). A solution of the acid chloride in dry acetone (25 c.c.) was added dropwise during 30 minutes to a vigorously stirred solution of sodium azide (18 g.) in water (30 c.c.) and acetone (30 c.c.) kept below 0° during the addition. After a further 20 minutes' stirring water and crushed ice were added and the azide was extracted from the mixture with benzene. The benzene extract was washed once with cold water and then dried ($CaCl_2$). The dry solution was cautiously heated on a water-bath until the evolution of nitrogen had ceased. The mixture was cooled and concentrated hydrochloric acid (30 c.c.) added. The mixture was again heated on a water-bath until the evolution of carbon dioxide had ceased. The benzene layer was separated and washed with water. The combined aqueous extracts were made strongly alkaline with aqueous potassium hydroxide (40%), and the liberated amine extracted with benzene. After removal of the benzene from the dried (K_2CO_3) extract, the residue was distilled under reduced pressure to give 2-phenyl-*n*-propylamine (19·5 g.; b. p. 102—103°/17 mm.). Von Braun, Grabowski, and Kirschbaum (*Ber.*, 1913, **46**, 1280) obtained this amine by means of a Hofmann reaction on β-phenyl-*n*-butyramide and record b. p. 104°/21 mm.

2-p-*Chlorophenylethylamine.* β-*p*-Chlorophenylpropionic acid (10 g.; Skraup and Schwamberger, *Annalen*, 1928, **462**, 147), treated under identical conditions to those given above, proportional quantities being used, gave 2-*p*-chlorophenylethylamine (7·5 g.; b. p. 114—116°/15 mm.). The *hydrochloride* crystallised from concentrated hydrochloric acid in plates, m. p. 215° (Found: C, 49·9; H, 6·0. $C_8H_{10}NCl,HCl$ requires C, 50·0; H, 5·8%).

1-3′ : 4′-*Methylenedioxyphenyl-2-propylamine.* α-Piperonylpropionic acid (27 g.; Lorenz, *Ber.*, 1880, **13**, 760) was treated with an excess of phosphorus trichloride and after the vigorous reaction had subsided the mixture was heated to 60° for 2 hours. The excess of phosphorus trichloride was distilled from the mixture under reduced pressure, and the acid chloride extracted from the residue with dry ether and added with shaking to aqueous ammonia (*d* 0·88) in large excess. The mixture was heated on a water-bath to remove the ether and then chilled. The *amide* (26 g.) was filtered off from the solution. A sample separated from aqueous alcohol in plates, m. p. 121° (Found: C, 63·3; H, 6·6. $C_{11}H_{13}O_3N$ requires C, 63·4; H, 6·3%). A cold solution of alkaline sodium hypochlorite was prepared by absorbing chlorine (5·5 g.) in a solution of sodium hydroxide (20 g.) in water (50 c.c.) and crushed ice (100 g.). To this mechanically stirred solution was added the above powdered crude amide (25·5 g.). After 10 minutes the temperature was slowly raised to 50° and a solution of potassium hydroxide (36 g.) in water (200 c.c.) was slowly added. When all the amide had dissolved the mixture was again heated to 70° and kept at 70—80° for half an hour, during which an oil commenced to separate from the solution. The mixture was cooled and extracted with benzene. After removal of benzene from the dried (K_2CO_3) extract, the residue was distilled under reduced pressure to give 1-3′ : 4′-methylenedioxyphenyl-2-propylamine (9·5 g.; b. p. 149—150°/14 mm.). Merck (D.R.-P. 274,350) describes the preparation of this amine by the addition of hydrogen bromide to safrole followed by amination, and records b. p. 153°/19 mm.

Nicotinoyl and iso*Nicotinoyl Chloride Hydrochlorides.*—The preparation of the hydrochlorides of nicotinoyl and *iso*nicotinoyl chloride has been described by Späth and Spitzer (*Ber.*, 1926, **59**, 1477). In the present work these acid chloride hydrochlorides were freshly prepared before use by heating a mixture of the acid and thionyl chloride under reflux for 2 hours. The excess of thionyl chloride was distilled from the mixture, and the acid chloride hydrochloride purified by sublimation under reduced pressure.

Preparation of the Amides.—The powdered nicotinoyl (or *iso*nicotinoyl) chloride hydrochloride (0·03 mol.) was added during 2 minutes to a solution of the base (0·09 mol.) in dry chloroform (50 c.c.). A vigorous reaction commenced almost immediately, which was completed by boiling the mixture under reflux for 2 hours on the water-bath. When cold, the mixture was shaken with water (25 c.c.), and the chloroform layer separated. After removal of the solvent the residue was crystallised. A quantity of the base was recovered from the aqueous extract. The amides prepared by this general procedure are listed in the following Table. The yields obtained varied from 60 to 85% calculated on the acid chloride hydrochloride.

N-*Substituted nicotin- and* iso*nicotin-amides.*

Amide.	M. p.	Cryst. form.	Formula.	Found, % C.	Found, % H.	Reqd., % C.	Reqd., % H.
N-Nicotinoyl-2-phenylethylamine	79°	needles [a]	$C_{14}H_{14}ON_2$	74·1	6·0	74·3	6·2
*N-iso*Nicotinoyl-2-phenylethylamine	123	needles [b]	,,	74·0	6·1	,,	,,
N-Nicotinoyl-1-phenyl-2-propylamine	98	needles [c]	$C_{15}H_{16}ON_2$	75·1	6·6	75·0	6·6
*N-iso*Nicotinoyl-1-phenyl-2-propylamine	109	needles [b]	,,	75·1	6·6	,,	,,
N-Nicotinoyl-2-phenyl-*n*-propylamine	73	needles [d]	$C_{15}H_{16}ON_2$	75·2	6·5	75·0	6·6
*N-iso*Nicotinoyl-2-phenyl-*n*-propylamine	83	needles [d]	,,	75·1	6·4	,,	,,
N-Nicotinoyl-2-*p*-methoxyphenylethylamine	116	needles [b]	$C_{15}H_{16}O_2N_2$	70·3	6·7	70·3	6·3
*N-iso*Nicotinoyl-2-*p*-methoxyphenylethylamine	130	plates [a]	,,	70·2	6·4	,,	,,
N-Nicotinoyl-2-(3 : 4-methylenedioxyphenyl)-ethylamine	129	needles [f]	$C_{15}H_{14}O_3N_2$	66·7	5·6	66·7	5·2
*N-iso*Nicotinoyl-2-(3 : 4-methylenedioxyphenyl)ethylamine	138	needles [f]	,,	66·7	5·4	,,	,,
N-Nicotinoyl-1-(3 : 4-methylenedioxyphenyl)-2-propylamine	120 [*]	needles [e]	$C_{16}H_{16}O_3N_2$	67·5	5·6	67·6	5·7
N-Nicotinoyl-2-*p*-chlorophenylethylamine	133	plates [a]	$C_{14}H_{13}ON_2Cl$	64·9	4·7	64·5	5·05
*N-iso*Nicotinoyl-2-*p*-chlorophenylethylamine	108	needles [a]	,,	64·8	4·9	,,	,,

Solvents: *a*, light petroleum (b. p. 80—100°); *b*, benzene–light petroleum (b. p. 60—80°); *c*, ether; *d*, ether–light petroleum (b. p. 40—60°); *e*, benzene–light petroleum (b. p. 80—100°); *f*, benzene.

[*] D.R.-P. 549,967 records m. p. 99—100° for this amide.

3 : 4-*Dihydro*-1-3′-*pyridylisoquinoline*.—A mixture of *N*-nicotinoyl-2-phenylethylamine (4·4 g.) and phosphorus pentachloride (5·1 g.) was warmed whereupon a vigorous reaction set in. The mixture was gently heated on a water-bath for a further 20 minutes. Thiophen-free benzene (25 c.c.) was then added and the mixture shaken until the yellow oil had dissolved. Aluminium chloride (5 g.) was then added in one portion. When the vigorous reaction had subsided the mixture was heated on a water-bath for 3 hours. The dark brown resulting mixture was poured on crushed ice, and the aqueous solution extracted with ether. Concentrated hydrochloric acid (20 c.c.) was added and the mixture boiled under reflux for 12 hours in order to hydrolyse any unchanged starting material. After being boiled with animal charcoal and filtered, the colourless filtrate was made strongly alkaline with aqueous sodium hydroxide (20%). The liberated oil was extracted with ether and dried (K_2CO_3). After removal of the ether distillation under reduced pressure gave 3 : 4-*dihydro*-1-3′-*pyridylisoquinoline* (2·7 g.; b. p. 118°/8·3 × 10^{-3} mm.) (Found : N, 13·2. $C_{14}H_{12}N_2$ requires N, 13·45%). The *dipicrate*, prepared in the normal manner, separated from acetone–methyl alcohol in fine yellow needles, m. p. 192° after having first sintered at 160° (Found : C, 46·7; H, 2·9. $C_{14}H_{12}N_2,2C_6H_3O_7N_3$ requires C, 46·8; H, 2·7%).

3 : 4-*Dihydro*-1-4′-*pyridylisoquinoline*.—*N-iso*Nicotinoyl-2-phenylethylamine (5·4 g.) was cyclised under conditions identical with those described above, using phosphorus pentachloride (6·25 g.) and aluminium chloride (6 g.) in benzene (30 c.c.). 3 : 4-*Dihydro*-1-4′-*pyridylisoquinoline* (3·5 g.; b. p. 132—135°/1·3 × 10^{-4} mm.) was obtained as a viscous oil (Found : N, 12·9%). The *dipicrate* separated from dioxan in orange needles, m. p. 146—147° (decomp.) (Found : C, 46·4; H, 3·1%).

The following preparations are analogous : 3 : 4-*Dihydro*-3-*methyl*-1-3′-*pyridylisoquinoline* (2·5 g.), from *N*-nicotinoyl-1-phenyl-2-propylamine (3·1 g.), phosphorus pentachloride (3·5 g.), and aluminium chloride (4 g.) in benzene (25 c.c.), had b. p. 106—108°/3 × 10^{-3} mm. (Found : N, 12·9. $C_{15}H_{14}N_2$ requires N, 12·6%). The *dipicrate* separated from acetone in yellow needles, m. p. 161—162° (Found : C, 47·6; H, 2·9. $C_{15}H_{14}N_2,2C_6H_3O_7N_3$ requires C, 47·7; H, 3·0%).

3 : 4-*Dihydro*-3-*methyl*-1-4′-*pyridylisoquinoline* (2·9 g.), from *N-iso*nicotinoyl-1-phenyl-2-propylamine (3·5 g.), phosphorus pentachloride (4 g.), and aluminium chloride (4·3 g.) in thiophen-free benzene (30 c.c.), had b. p. 122—125°/3 × 10^{-3} mm., and solidified on cooling and separated from light petroleum (b. p. 60—80°) in fine needles, m. p. 58° (Found : N, 12·2%). The *dipicrate* separated from acetone in fine needles, m. p. 126—127° (Found : C, 47·5; H, 3·2%).

3 : 4-*Dihydro*-4-*methyl*-1-3′-*pyridylisoquinoline* (3·1 g.), from *N*-nicotinoyl-2-phenyl-*n*-propylamine (6·8 g.), phosphorus pentachloride (7·75 g.), and aluminium chloride (9 g.) in benzene (40 c.c.), had b. p. 136—138°/9·3 × 10^{-4} mm. (Found : N, 12·2%). The *dipicrate* separated from acetone–methyl alcohol in fine needles, m. p. 151° (decomp.) (Found : C, 47·3; H, 3·1%).

3 : 4-*Dihydro*-4-*methyl*-1-4′-*pyridylisoquinoline* (2·9 g.), from *N-iso*nicotinoyl-2-phenyl-*n*-propylamine (6·5 g.), phosphorus pentachloride (7·5 g.), and aluminium chloride (8·8 g.) in benzene (40 c.c.), had b. p. 138°/1·5 × 10^{-4} mm. and crystallised when kept and separated from light petroleum (b. p. 60—80°) in hard needles, m. p. 82° (Found : N, 12·2%). The *dipicrate* separated from acetone–methyl alcohol in fine needles, m. p. 172° (decomp.) (Found : C, 47·8; H, 3·1%).

1-3′-*Pyridylisoquinoline*.—3 : 4-Dihydro-1-3′-pyridylisoquinoline (2·6 g.) was dehydrogenated by heating it at 240—250° for 30 minutes with palladium–charcoal (0·3 g.; 10%). The mixture was extracted with benzene and filtered. After removal of the solvent the solid residue was recrystallised from light petroleum (b. p. 40—60°). 1-3′-*Pyridylisoquinoline* (2·1 g.) separated in fine needles, m. p. 58° (Found : C, 81·6; H, 5·3. $C_{14}H_{10}N_2$ requires C, 81·5; H, 4·9%). The *dipicrate* separated from acetone–methyl alcohol in plates, m. p. 192—193° (Found : C, 46·7; H, 2·4. $C_{14}H_{10}N_2,2C_6H_3O_7N_3$ requires C, 47·0; H, 2·4%).

Similar dehydrogenations led to the following : 1-4′-*Pyridylisoquinoline* (2·9 g. from 3·3 g.) separated from light petroleum (b. p. 80—100°) in fine needles, m. p. 89° (Found : C, 81·4; H, 5·1%). The *picrate* separated from dioxan in fine needles, m. p. 205° after having sintered at 170° (Found : C, 55·5; H, 3·1. $C_{14}H_{10}N_2,C_6H_3O_7N_3$ requires C, 55·2; H, 3·0%).

3-*Methyl*-1-3′-*pyridylisoquinoline* (1·9 g. from 2·3 g.) separated from light petroleum (b. p. 60—80°) in fine needles, m. p. 94° (Found : C, 82·1; H, 5·35. $C_{15}H_{12}N_2$ requires C, 81·8; H, 5·5%). The *dipicrate* separated from methyl alcohol in fine needles, m. p. 172° after having sintered at 156° (Found : C, 48·1; H, 2·7. $C_{15}H_{12}N_2,2C_6H_3O_7N_3$ requires C, 47·8; H, 2·8%).

3-*Methyl*-1-4′-*pyridylisoquinoline* (2·1 g. from 2·8 g.) separated from light petroleum (b. p. 80—100°) in needles, m. p. 117° (Found : C, 82·0; H, 5·4%). The *picrate* separated from dioxan–*cyclo*hexanone in fine needles, m. p. 251—254° after having sintered at 210° (Found : C, 56·2; H, 3·6. $C_{15}H_{12}N_2,C_6H_3O_7N_3$ requires C, 56·1; H, 3·4%).

4-*Methyl*-1-3′-*pyridylisoquinoline* (2·5 g. from 3 g.) had b. p. 128°/5 × 10^{-4} mm. (Found : C, 81·1; H, 6·1%). The *picrate* separated from dioxan in needles, m. p. 123—124° (Found : C, 56·2; H, 3·2%). 4-*Methyl*-1-4′-*pyridylisoquinoline* (1·1 g. from 1·5 g.) had b. p. 136—137°/2·5 × 10^{-4} mm. and separated from light petroleum (b. p. 80—100°) in fine needles, m. p. 113° (Found : C, 82·1; H, 5·2%). The *picrate* separated from dioxan in needles, m. p. 235—237° after having sintered at 185° (Found : C, 56·1; H, 3·1%).

7-*Chloro*-3 : 4-*dihydro*-1-3′-*pyridylisoquinoline*.—*N*-Nicotinoyl-2-*p*-chlorophenylethylamine could not be cyclised with phosphoric oxide in boiling xylene. The amide (2·1 g.) was, however, cyclised by conversion into the imidochloride with phosphorus pentachloride (2·0 g.), followed by treatment with aluminium chloride (2·0 g.) in benzene (50 c.c.). 7-*Chloro*-3 : 4-*dihydro*-1-3′-*pyridylisoquinoline* (1·1 g.; b. p. 151—155°/2·7 × 10^{-4} mm.) separated from ether–light petroleum (b. p. 40—60°) in cubic crystals, m. p. 92° (Found : C, 69·0; H, 4·65. $C_{14}H_{11}N_2Cl$ requires C, 69·3; H, 4·6%). The *dipicrate* separated from acetone–methyl alcohol in fine needles, m. p. 175° having sintered at 145° (Found : C, 44·7; H, 2·9. $C_{14}H_{11}N_2Cl,2C_6H_3O_7N_3$ requires C, 44·5; H, 2·4%).

7-*Chloro*-3 : 4-*dihydro*-1-4′-*pyridylisoquinoline* (0·9 g. from 2·1 g.), prepared and purified similarly, formed cubic crystals, m. p. 113° (Found : C, 69·3; H, 4·7%). The *dipicrate* separated from alcohol in needles, m. p. 151° (decomp.) (Found : C, 44·5; H, 3·0%).

3 : 4-*Dihydro*-6 : 7-*methylenedioxy*-1-3′-*pyridylisoquinoline*.—*N*-Nicotinoyl-2-(3 : 4-methylenedioxyphenyl)ethylamine (3·5 g.) and phosphorus pentachloride (3·0 g.) were warmed together on a water-bath for 10 minutes. Pure xylene (30 c.c.) was then added and the mixture boiled under reflux in an oil-bath for 1 hour. The cold mixture was shaken with water (50 c.c.), and the aqueous layer separated from the xylene fraction. The base was liberated from the aqueous solution by the addition of aqueous sodium hydroxide and extracted with benzene. After removal of the solvent the residue crystallised and repeated crystallisation from benzene gave 3 : 4-*dihydro*-6 : 7-*methylenedioxy*-1-3′-*pyridylisoquinoline* (1·3 g.) in rectangular prisms, m. p. 130° (Found : N, 10·8. $C_{15}H_{12}O_2N_2$ requires N, 11·1%). The *dipicrate* separated from acetone in needles, m. p. 183—184° (Found : C, 46·1; H, 2·7. $C_{15}H_{12}O_2N_2,2C_6H_3O_7N_3$ requires C, 45·6; H, 2·5%). An attempt to dehydrogenate this compound with palladium–charcoal at 220° led to complete disintegration.

3 : 4-*Dihydro*-6 : 7-*methylenedioxy*-1-4′-*pyridylisoquinoline*.—*N*-*iso*Nicotinoyl-2-(3 : 4-methylenedioxyphenyl)ethylamine (3·5 g.) was cyclised under identical conditions to the *dihydroisoquinoline* (1·1 g.), which separated from ether in fine needles, m. p. 101—102° (Found : N, 11·5%). The *dipicrate* separated from acetone–methyl alcohol in needles, m. p. 210° after having sintered at 160° (Found : C, 45·4; H, 2·8%). Attempted dehydrogenation of this compound by palladium–charcoal led to complete disintegration.

3 : 4-*Dihydro*-3-*methyl*-6 : 7-*methylenedioxy*-1-3′-*pyridylisoquinoline*.—*N*-Nicotinoyl-1-(3 : 4-methylene dioxyphenyl)-2-propylamine (4 g.) and phosphorus pentachloride (3·3 g.) were warmed together and then heated in an oil-bath for 1 hour in xylene (30 c.c.). The dihydro*iso*quinoline (1·7 g.; b. p. 165—167°/7 × 10^{-4} mm.) was isolated in the normal manner and separated from ether in needles, m. p. 135° (Found : C, 72·3; H, 5·0. Calc. for $C_{16}H_{14}O_2N_2$: C, 72·2; H, 5·3%). The *dipicrate* separated from alcohol in needles, m. p. 200° after having sintered at 190° (Found : C, 46·0; H, 2·8. $C_{16}H_{14}O_2N_2,2C_6H_3O_7N_3$ requires C, 46·4; H, 2·8%).

6 : 7-*Methylenedioxy*-1-3′-*pyridylisoquinoline*.—To a boiling solution of 3 : 4-dihydro-6 : 7-methylenedioxy-1-3′-pyridyl*iso*quinoline (0·5 g.) in dioxan (20 c.c.), bromine (0·1 c.c.) was added in one portion. The mixture was boiled for a further 20 seconds and then rapidly cooled. After cooling at 5° for 1 hour the crystalline 6 : 7-methylenedioxy-1-3′-pyridyl*iso*quinoline hydrobromide was filtered off and decomposed with aqueous ammonia. The liberated base was extracted with benzene and after removal of the solvent the solid residue crystallised from light petroleum (b. p. 80—100°), containing a trace of benzene, in fine needles, m. p. 186° (Found : C, 72·4; H, 3·9. $C_{15}H_{10}O_2N_2$ requires C, 72·0; H, 4·0%). The *dipicrate* separated from acetone–methyl alcohol in fine needles, m. p. 200° after having sintered at 180° (Found : C, 45·6; H, 2·3. $C_{15}H_{10}O_2N_2,2C_6H_3O_7N_3$ requires C, 45·7; H, 2·3%).

3-*Methyl*-6 : 7-*methylenedioxy*-1-3′-*pyridylisoquinoline*.—3 : 4-Dihydro-3-methyl-6 : 7-methylenedioxy-1-3′-pyridyl*iso*quinoline was dehydrogenated with palladium–charcoal as described in D.R.-P. 549,967. The base was purified by sublimation under reduced pressure, followed by recrystallisation from light petroleum (b. p. 80—100°), from which solvent it separated in fine needles, m. p. 190—191° (Found : C, 72·5; H, 4·3. Calc. for $C_{16}H_{12}O_2N_2$: C, 72·7; H, 4·6%). The *dipicrate* separated from acetone–methyl alcohol in fine needles, m. p. 192° (Found : C, 46·7; H, 2·3. $C_{16}H_{12}O_2N_2,2C_6H_3O_7N_3$ requires C, 46·5; H, 2·5%). D.R.-P. 549,967 records m. p. 192° for the free base.

Methyl o-3-*Pyridylbenzoate*.—A mixture of methyl anthranilate (15 g.), suspended in concentrated hydrochloric acid (30 c.c.) and crushed ice (25 g.) and externally cooled by ice–salt, was diazotised with aqueous sodium nitrite (16 g.), and the resulting solution was dropped as rapidly as possible into stirred pyridine (150 c.c.) at 40—50°. The temperature of the mixture was then gradually raised to 70° and kept at this temperature for 0·5 hour for completion of the reaction. An aqueous solution of sodium carbonate (16 g.; anhydrous) was then added and the excess of pyridine removed with steam. The cooled mixture was extracted with ether, the ethereal extract was dried (K_2CO_3), and after removal of the ether the residue was distilled under reduced pressure. The fraction (10·5 g.), b. p. 110—120°/1·3 × 10^{-2} mm., was dissolved in acetone (300 c.c.) and to the hot solution picric acid (12 g.) was added. When cold a mixture of methyl *o*-3-pyridylbenzoate picrates (12 g.) separated in clusters of fine needles, m. p. 188—189°. After a number of crystallisations from the same solvent the *picrate* of methyl *o*-3-pyridylbenzoate melted at 192—193° (Found : C, 51·8; H, 3·4. $C_{13}H_{11}O_2N,C_6H_3O_7N_3$ requires C, 51·6; H, 3·2%). The picrate (10 g.) was decomposed by adding it to a hot, mechanically stirred mixture of aqueous sodium hydroxide (5%) and benzene. The benzene extract was dried (K_2CO_3) and, after removal of the benzene, the residue was distilled under reduced pressure to give methyl *o*-3-pyridylbenzoate (4 g.; b. p. 114—117°/1·3 × 10^{-2} mm.). A sample (0·5 g.) was hydrolysed in boiling alcoholic sodium hydroxide. After removal of the alcohol under reduced pressure, the residue was ground with soda-lime and strongly heated in an attempt to effect decarboxylation. The neutral product which distilled from the mixture was converted into its picrate and recrystallisation from alcohol gave the *dipicrate* of 2 : 2′-(di-3-pyridyl)benzophenone, which separated in fine needles, m. p. 197° (Found : C, 53·8; H, 3·0. $C_{23}H_{16}ON_2,2C_6H_3O_7N_3$ requires C, 53·2; H, 2·8%).

3-*o*-*Cyanophenylpyridine*.—3-*o*-Aminophenylpyridine (4 g.; b. p. 128°/6 × 10^{-4} mm.; m. p. 52°; Coates *et al.*, *loc. cit.*) was diazotised in concentrated hydrochloric acid (10 c.c.) and water (10 c.c.) at 0—5° with aqueous sodium nitrite (2 g.) in water (5 c.c.). The solution of the diazonium salt was slowly added to a well-stirred suspension of nickel cyanide (7·5 g.) in water (20 c.c.) to which potassium cyanide (20 g.) had been added. After the addition the mixture was heated on a steam-bath for 20 minutes. The hot solution was filtered from tar and cooled, whereupon a small quantity of the nitrile separated. The tar was extracted with methyl alcohol and the solution boiled with animal charcoal and filtered. Concentration of the filtrate and dilution with water gave a further quantity of the crude nitrile. 3-*o*-*Cyanophenylpyridine* (2·2 g.) separated from methyl alcohol in fine needles, m. p. 89° (Found : C 80·0; H, 4·6. $C_{12}H_8N_2$ requires C, 80·0; H, 4·5%).

o-3-*Pyridylbenzoic Acid.*—3-*o*-Cyanophenylpyridine (2·1 g.) was hydrolysed in boiling alcoholic potassium hydroxide under reflux for 12 hours. The alcohol was distilled from the mixture on a water-bath, and the solid residue dissolved in the minimum of hot water. The free acid liberated from this solution on acidification with acetic acid was recrystallised from aqueous methyl alcohol, to give 2-3′-pyridylbenzoic acid (2·1 g.) in needles, m. p. 185°. Skraup (*Monatsh.*, 1884, **4**, 450) records m. p. 185° for this acid, obtained by the decarboxylation of 3-*o*-carboxyphenylpyridine-2-carboxylic acid. The methyl ester was prepared by heating a mixture of the acid (1 g.), methyl alcohol (20 c.c.) and concentrated sulphuric acid (3 g.) on a steam-bath for 4 hours. The mixture was poured on crushed ice, and the ester extracted with ether after neutralisation with aqueous ammonia. After evaporation of the ether, the residual oil was dissolved in acetone (50 c.c.) and to the hot solution, a hot solution of picric acid (1 g.) in acetone (10 c.c.) was added. On cooling, the picrate of methyl *o*-3-pyridylbenzoate separated in clusters of fine needles, m. p. 191—192°, not depressed when mixed with a sample of the picrate prepared as described above.

A mixture of methyl 2-3′-pyridylbenzoate (4 g.), alcohol (4 c.c.), and hydrazine hydrate (2 c.c.; 90%) was heated on a water-bath for 1 hour. Removal of the alcohol under reduced pressure left a viscous residue (3·6 g.), which solidified in a desiccator ($CaCl_2$). o-3-*Pyridylbenzoylhydrazide*, which was obtained in almost quantitative yield, separated from alcohol in plates, m. p. 138° (Found: C, 67·4; H, 5·4. $C_{12}H_{11}ON_3$ requires C, 67·6; H, 5·2%).

To a solution of the hydrazide (3·5 g.) in pyridine (10 c.c.) was added toluene-*p*-sulphonyl chloride (3·5 g.), and the mixture was heated to 80° for 1 hour. When the mixture was poured into water N-o-3-*pyridylbenzoyl*-N-*toluene*-p-*sulphonhydrazide* was precipitated in almost quantitative yield as a white crystalline compound, which separated from alcohol in fine needles, m. p. 220° (Found: C, 61·8; H, 5·4. $C_{19}H_{17}O_3N_3S$ requires C, 62·1; H, 4·6%).

o-3-*Pyridylbenzaldehyde.*—To a solution of the above toluene-*p*-sulphonyl derivative (5·5 g.) in glycol (50 c.c.) at 150°, anhydrous sodium carbonate (5·5 g.) was added in one portion, and the mixture kept at 150° for 3 minutes. After rapid cooling, the mixture was poured on crushed ice and extracted with chloroform (4 × 30 c.c.). After removal of the solvent from the dried extract (K_2CO_3), the residue was distilled under reduced pressure to give o-3-*pyridylbenzaldehyde* (1·85 g.; b. p. 117°/7·28 × 10^{-4} mm.), which separated from light petroleum (b. p. 60—80°) in fine needles, m. p. 63° (Found: C, 78·65; H, 5·1. $C_{12}H_9ON$ requires C, 78·65; H, 5·0%).

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351. *The Absorption Spectra of Some Cellulose Derivatives in the 3-μ. Region.*

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The infra-red absorption spectra of native and regenerated cellulose and of a number of cellulose derivatives have been measured in the region 2·5—4·0 μ. The results show that the shape and frequency of the absorption band associated with the fundamental hydroxyl stretching mode give considerable information about the hydrogen-bonding conditions, and in particular may be used as a criterion of uniformity of substitution along the cellulose chains. The possibility of using the intensity of the hydroxyl band as a measure of the hydroxyl content of cellulose derivatives is discussed. Preliminary infra-red measurements are described on the water imbibition of some cellulose ethers and esters.

It is generally accepted that a reaction involving fibrous cellulose will proceed more rapidly in the less crystalline regions, and the highly crystalline material will only react to an equivalent extent if one of three conditions is fulfilled, namely: (i) the reaction goes to completion, giving a trisubstituted derivative; (ii) an equilibrium is set up, the extent of the reaction depending on the concentration of reagents; (iii) the cellulose passes into solution or becomes so highly swollen that all distinction between the regions of varying crystallinity is lost.

In the preparation of incompletely substituted cellulose esters of organic acids the first and third of these conditions are used, a substantially completely substituted product, the primary ester, being subjected to partial hydrolysis in solution, thus ensuring a uniformly substituted secondary ester. If, however, the substitution stops short of the triester, the unesterified material will consist largely of the more crystalline parts of the cellulose, and in the resulting

secondary ester the degree of substitution will vary for different portions of the same chain. Such non-uniform substitution will have a marked effect on the solubility properties, since the normal solvents for cellulose esters are incapable of solvating those portions of the chain where the packing differs little from that found in crystalline cellulose. Where, however, these regions are small compared with the substituted regions, it is possible that the material will dissolve in the normal solvents, but that the resulting solution will show poor flow properties and give an apparent viscosity greater than that indicated by the average molecular weight of the solute. Similar considerations apply to the solubility of cellulose ethers.

As there are other explanations of the anomalous solubility properties of certain cellulose derivatives, a method was sought for the direct detection of non-uniform substitution as distinct from the chemical methods used by Purves and his collaborators (*J. Amer. Chem. Soc.*, 1939, **61**, 3458, 3463; 1942, **64**, 9, 15, 1539). The measurement of the infra-red absorption spectra seemed to offer some hope of an unambiguous solution, as non-uniform substitution will cause variations in the hydrogen-bonding conditions around the residual hydroxyl groups and such variations should affect the hydroxyl-stretching frequency near 3 μ.

Experimental.

The spectra were measured on a Hilger D.209 double-beam recording spectrometer fitted with a lithium fluoride prism. The slit width used was 0·2 mm. and the accuracy of the frequency measurements was probably better than ±3 cm.$^{-1}$. The quantitative measurements on the intensity of the hydroxyl absorption were made on a Grubb–Parsons S-3 single-beam spectrometer, a sodium chloride prism and slit width of 0·026 mm. being used.

The cellulose derivatives were studied in the form of films of suitable thickness cast from the appropriate solvents on glass plates. The regularity of most of the films cast this way is so great as to give interference fringes in the infra-red, which appear as spurious absorption bands. The production of these undesirable fringes was eliminated by casting the films on finely ground glass plates.

To avoid the effects of absorbed water, the films were measured in the dry state. The water content of fibres and films of thicknesses suitable for infra-red investigation reaches equilibrium with the surrounding atmosphere in a matter of a minute or so. To obtain the spectrum of a dry sample it is therefore essential that the atmosphere in contact with the specimen should be kept dry throughout a measurement. This can be achieved in several ways: (i) by mounting the film in a cell which can be evacuated; (ii) by mounting the film in a sealed cell containing phosphoric oxide or magnesium perchlorate; or (iii) by mounting the film in a cell through which a stream of dry nitrogen can be passed. It was found that a combination of (i) and (ii) gave the most rapid drying. The cell used was made of brass, with rock-salt windows, and was small enough to be located at the primary focus of the Grubb–Parsons S-3 spectrometer. A small tray of phosphoric oxide was included in the cell, and an outlet tube attached to a pump allowed the cell to be kept under vacuum throughout an experiment. Under these conditions no further change in the spectrum of any of the samples could be detected after about 5 minutes. The position of the film mount could be adjusted externally by means of a screw, so that measurements could be made through various portions of the film without breaking the vacuum.

Results and Discussion.

(a) *Native and Regenerated Cellulose.*—The spectrum of native cellulose from 2700 to 3700 cm.$^{-1}$ is shown in Fig. 1, No. 1. The results, obtained from two different thicknesses of the cell wall of *Valonia ventricosa*, refer to undried samples but it was found that subjection of the films to an intensive drying treatment produced no detectable change in the spectrum. When the sample was heated in a stream of hot, dry nitrogen the bands were reduced in intensity and shifted to higher frequencies, a shift of some 20 cm.$^{-1}$ being observed for the 3350-cm.$^{-1}$ band at about 150°, but when the nitrogen stream was cooled the spectrum reverted to that of an undried sample. The CH band shows three well-resolved peaks, and the hydroxyl band three peaks at 3245, 3274, and 3350 cm.$^{-1}$ with a shoulder on each side of the 3350-cm.$^{-1}$ band.

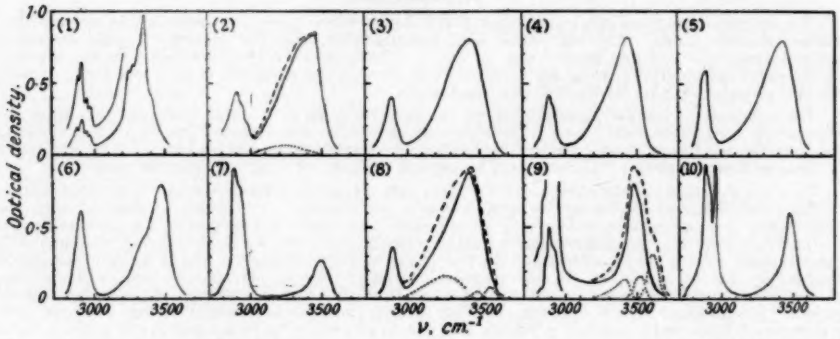
The spectrum of regenerated cellulose (Fig. 1, No. 2), obtained from a sample of viscose film, is in marked contrast to that of *Valonia*, the CH absorption being less well resolved and the OH band broad and ill defined. Further, there is a detectable change in the OH absorption on drying. It is known from *X*-ray diffraction results, and in particular from the measurements by Hermans and Weidinger (*J. Polymer Sci.*, 1949, **4**, 135), that *Valonia* is much more crystalline than regenerated cellulose. It is also known that water cannot be absorbed in the lattice of native cellulose, but that regenerated cellulose readily forms a hydrated lattice in moist air (*idem*, *J. Colloid Sci.*, 1946, **1**, 185). The sharpness of the OH and CH bands in *Valonia*, and the apparent absence of absorbed water, agrees with these results. The less well-resolved CH bands and the broad OH absorption in the viscose film are in agreement with a much lower degree of crystallinity. The spectrum of the absorbed water is discussed in the next section.

(b) *Cellulose Cyanoethyl Ethers.*—The possibility of obtaining a correlation between the

solubility and the hydroxyl absorption of cellulose derivatives was first investigated for a series of cyanoethyl ethers, this class of compound being chosen because samples prepared by MacGregor's method (B.P. 588,751, 605,357) were available over a wide substitution range. The cyanoethyl celluloses do not, however, constitute an ideal case for an investigation of this type, because in their preparation some hydrolysis of the cyano-groups always occurs. Spectroscopic measurements have shown that this hydrolysis usually stops at the amide stage and involves only a small proportion of the cyano-groups. In the present considerations the presence of amido-groups may be ignored.

The degree of substitution of a cellulose derivative may be defined as the average number of hydroxyl groups substituted per anhydroglucose residue. On this basis the degree of substitution of a fully substituted cellulose derivative is 3. At low degrees of substitution the cyanoethyl celluloses are soluble in dilute solutions of sodium hydroxide and the hydroxyl absorption is similar to that of regenerated cellulose. This is illustrated in Fig. 1, Nos. 8 and 3, where the spectra of two derivatives of degree of substitution 0·15 and 0·66 are shown. At the higher degree of substitution it is possible to prepare water-soluble derivatives, the spectrum of

FIG. 1.



Curve no.	*Substance.*	*Curve no.*	*Substance.*
1	Valonia ventricosa.	6	*Cyanoethyl cellulose* (2·12).
2	*Regenerated cellulose.*	7	*Cyanoethyl cellulose* (2·96).
3	*Cyanoethyl cellulose* (0·66).	8	*Cyanoethyl cellulose* (0·15).
4	*Cyanoethyl cellulose* (0·77).	9	*Cyanoethyl cellulose* (2·92).
5	*Cyanoethyl cellulose* (2·00).	10	*Cellulose ether.*

Figures in parentheses refer to degree of substitution.

- - - - *Undried samples.* ——— *Dried samples.*

such a substance of degree of substitution 0·70 being shown in Fig. 1, No. 4. The maximum of the OH absorption is a few wave-numbers higher for the water-soluble cyano-ether and the band is more symmetrical than that of the alkali-soluble cyano-ether. In cellulose and its derivatives, where there are regions of varying crystallinity, corresponding hydroxyl groups will not all be similarly environed even for a uniform distribution of substituent groups, and the resulting OH band may probably be regarded as a type of distribution curve showing the proportions of hydroxyl groups with the various possible degrees of hydrogen bonding. The shape of the OH band is clearly of importance, as a small proportion of strongly hydrogen-bonded OH groups will have a considerable influence on the solubility characteristics. Some measure of the symmetry of the OH absorption bands may be obtained from the ratio of the band widths on the low- and on the high-frequency side of the maximum at half the peak optical density. This designation for symmetry being used, the symmetry index for a symmetrical band is unity and is greater than unity for bands which are broadened on the low-frequency side. The results obtained for a number of cyanoethyl celluloses are summarized in the table, from which it can be seen that the water-soluble derivatives show an OH frequency in the range 3450 $\pm$ 3 cm.$^{-1}$ and a symmetry index of between 1·5 and 1·9. For the alkali-soluble derivatives the corresponding figures are 3434 $\pm$ 12 cm.$^{-1}$ and 2·0—2·5, respectively. Regenerated cellulose has an OH frequency of 3443 cm.$^{-1}$ with a symmetry index of about 2·6. It is evident that the water-soluble cyanoethyl celluloses are less like regenerated cellulose in their state of

hydrogen bonding than are the alkali-soluble derivatives. This implies a greater penetration of the highly crystalline regions of the cellulose by the substituent groups in the former case; *i.e.*, the water-soluble cyano-ethers are more uniformly substituted than the alkali-soluble cyano-ethers.

Degree of substitution.	Solubility.	ν_{OH}, cm.$^{-1}$.	Symmetry index.	Degree of substitution.	Solubility.	ν_{OH}, cm.$^{-1}$.	Symmetry index.
0·00 *	—	3443	2·6	1·28	Aq. NaOH	3429	2·0
0·15	Aq. NaOH	3443	2·5	1·38	Aq. NaOH	3435	2·1
0·57	Aq. NH_3	3432	1·7	1·70	Aq. NaOH	3422	2·0
0·66	Aq. NaOH	3440	2·0	2·00	Aq. NaOH/ acetone	3430	2·3
0·70	Water	3448	1·7				
0·84	Water	3451	1·5	2·12	Aq. acetone	3460	1·7
0·90	Water	3453	1·8	2·70	Acetone	3476	1·1
1·05	Water	3448	1·9	2·79	Acetone	3477	1·0
1·05	Aq. NaOH	3437	2·1	2·92	Acetone	3484	1·1
1·10	Water	3453	1·5	2·92	Acetone	3481	1·0
1·21	Aq. NaOH	3435	2·5	2·96	Acetone	3481	1·0

* Regenerated cellulose.

When the degree of substitution exceeds a value of about 2, solubility in a purely aqueous medium would no longer be expected, and over the substitution range 2·0—2·5 it was found that the majority of the cyano-ethers were soluble in aqueous acetone; some, however, required the addition of alkali before dissolution would occur. The OH absorption of these two types of derivative is shown in Fig. 1, Nos. 5 and 6. The shapes of the two bands differ in the same way as was found in the lower substitution ranges, and the maxima differ by about 30 cm.$^{-1}$, the frequency of the alkali-soluble derivative being the lower one. Above a degree of substitution of about 2·6 the cyanoethyl celluloses are soluble in dry acetone and show an OH frequency of 3480 $\pm$ 4 cm.$^{-1}$ (Fig. 1, No. 7). The hydroxyl bands for these derivatives are almost symmetrical, the symmetry indices differing little from unity.

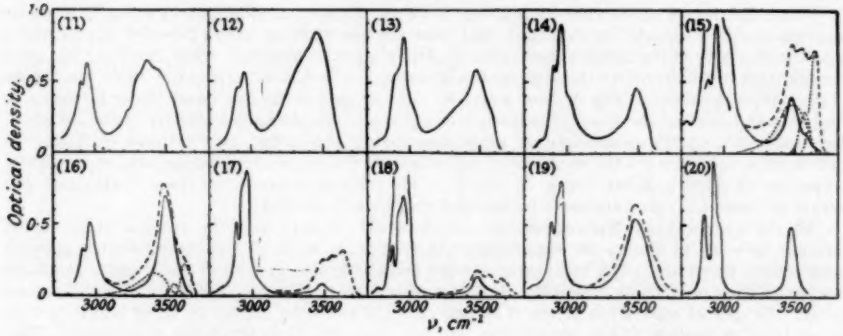
All the cyanoethyl celluloses readily absorb water vapour, and the spectra of the dried samples, referred to above, are appreciably different from those of the corresponding samples measured in moist air. The difference between the absorption spectra of a dry and an undried sample, plotted on an optical density versus frequency basis, gives the spectrum of the absorbed water. Graphical separation of the resulting curve shows it to consist of three bands, a very broad band extending to low frequencies and two sharper bands at higher frequencies. This is illustrated for two extreme samples in Fig. 1, Nos. 8 and 9. The broad low-frequency band is similar to that obtained with liquid water. The two high-frequency bands probably correspond to the symmetrical and antisymmetrical stretching frequencies of water molecules hydrogen-bonded to the hydrogen atoms of the cellulosic hydroxyl groups. It is difficult to make an accurate determination of the precise contour of the water absorption band, and from the nature of the graphical separation it is not possible to attach any great significance to variations in the frequencies of these three bands. It is, however, of interest that the absorption spectrum should serve to distinguish between bonded and non-bonded water. No evidence of the two high-frequency bands was obtained in the spectrum of regenerated cellulose. This difference between cellulose and the cyanoethyl celluloses is probably to be attributed to the fact that introduction of substituent groups must increase the spacing between adjacent chains. This will leave a number of unbonded hydroxyl groups which could form hydrogen bonds with water molecules. If this explanation of the observed differences is correct, it would seem that there can be very few unbonded OH groups in regenerated cellulose even in the less crystalline regions. This may be compared with the state of affairs found in polyamides where there is no spectroscopic evidence for any unbonded NH groups.

(c) *Cellulose Ethyl Ethers.*—All the cellulose ethyl ethers measured were in the substitution range 2·2—2·6. These samples showed similar solubility characteristics and in the dry state all showed a single OH band at 3479 cm.$^{-1}$. The spectrum of a typical cellulose ethyl ether is shown in Fig. 1, No. 10, and it can be seen that the CH absorption is appreciably different from that of a cellulose cyanoethyl ether.

(d) *Primary Cellulose Acetates.*—The results described for the cyanoethyl celluloses refer to the complete range of degrees of substitution. In order to obtain more detailed information about the hydrogen-bonding conditions, an investigation was made of a number of derivatives containing relatively few hydroxyl groups. This was done by studying the absorption spectra of a series of primary cellulose acetates, *i.e.*, cellulose acetates isolated during the later stages of the acetylation of cellulose.

The cellulose acetates investigated were isolated at hourly intervals from a fibrous acetylation. After the first hour the conditions of acetylation were such that the degree of substitution was of the order of 2·5, and thereafter it rose more slowly to a value of about 2·95. The early samples gave solutions in methylene chloride–alcohol which were of high viscosity and showed poor flow properties, whereas the later samples gave clear, oily solutions of progressively decreasing viscosity. The spectra of a selection of these acetates are shown in Fig. 2, Nos. 11—15. T_1, the earliest sample to be isolated, shows OH maxima at **3343** and at about **3455** cm.$^{-1}$ with shoulders at **3210** and **3290** cm.$^{-1}$. Comparison with the hydroxyl absorption in regenerated cellulose (Fig. 1, No. 2) shows that the main absorption at **3343** cm.$^{-1}$ is at a considerably lower frequency than that found in regenerated cellulose and is nearer to that found in native cellulose. This implies that the hydrogen-bonding conditions in some of the unesterified regions of T_1 must approximate closely to those found in the more highly crystalline parts of cellulose, and the presence of such regions of unattacked crystalline cellulose would account for the poor flow properties of T_1 in solution. T_2 and T_3 both show broad OH absorption bands with maxima at **3465** and **3470** cm.$^{-1}$, respectively. Both bands are

FIG. 2.



Curve no.	*Substance.*	*Curve no.*	*Substance.*
11	*Cellulose acetate T1* (2·5).	16	*Secondary cellulose acetate* (2·47).
12	*Cellulose acetate T2* (2·84).	17	*High-acetyl acetate butyrate.*
13	*Cellulose acetate T3* (2·87).	18	*Low-acetyl acetate butyrate.*
14	*Cellulose acetate T4* (2·91).	19	*Secondary acetate butyrate.*
15	*Cellulose acetate T5* (2·95).	20	*Cellulose laurate.*

Figures in parentheses refer to degree of substitution.

- - - - *Undried samples.* ——— *Dried samples.*

considerably broadened on the low-frequency side and show shoulders at about **3350** cm.$^{-1}$, and this again can be taken as evidence of the presence of crystalline cellulose, though in smaller quantity than in T_1. In T_4 the OH maximum is at **3480** cm.$^{-1}$ with shoulders at **3384** and **3558** cm.$^{-1}$. T_5 again shows a maximum at **3480** cm.$^{-1}$, but apart from the shoulder at **3558** cm.$^{-1}$ the absorption band is symmetrical and this type of hydroxyl absorption is typical of all the later members of the series. Hence, the spectroscopic results indicate a decrease in the amount of crystalline cellulose in passing from T_1 to T_4 and the absence of any such regions in T_5 and the subsequent members of the series, a decrease which is paralleled by the improved flow properties of solutions of these acetates in methylene chloride–alcohol.

In Fig. 2, No. 15 is shown the absorption spectrum of T_5 from **2700** to **3800** cm.$^{-1}$ for dried and undried samples. The undried sample shows three maxima of approximately equal intensity at **3485**, **3560**, and **3635** cm.$^{-1}$, while the dried sample only shows a single maximum at **3480** together with a shoulder at **3558** cm.$^{-1}$. Subtraction of the two absorption curves gives the absorption spectrum of the absorbed water, and graphical separation of this curve gives three peaks, as found with the cyanoethyl ethers. Again, it is probable that the two high-frequency bands are to be associated with hydrogen-bonded water, and the broad low-frequency band with absorbed liquid water. Although the shoulder at **3558** cm.$^{-1}$ in the spectrum of the dried sample is at the same frequency as one of the water bands, this shoulder cannot be removed on drying, and as the spectra of dried acetates show no evidence of the more intense water band

at 3635 cm.$^{-1}$, the shoulder must be due to some structural feature of the cellulose acetate molecule. From the frequency of this shoulder it is probably to be associated with unperturbed hydroxyl groups.

Examination of a molecular model of a portion of a cellulose acetate chain shows that if in any anhydroglucose unit the OH group in the 6 position is unsubstituted, the remaining two OH groups being substituted by acetyl radicals, then only a weak internal hydrogen bond with the bridge oxygen atom is possible. If, however, the free OH group is in the 2- or the 3-position, an internal hydrogen bond can be formed between the OH group and the adjacent carbonyl group. The existence of such an internal hydrogen bond would cause a certain stabilisation of the structure, and this stabilisation would probably account for Purves's results (*loc. cit.*) on the distribution of the unesterified hydroxyl groups in secondary cellulose acetates. He found that the number of glycol units in a secondary acetate was less than could be accounted for by a purely random hydrolysis, and concluded that in the partial hydrolysis from triacetate, the loss of an acetyl residue from the 2- or the 3-position tended to stabilise the adjacent group in the anhydroglucose residue. Thus it is possible that the shoulder at 3558 cm.$^{-1}$ is due to hydroxyl groups in the 6-position which are so environed as to be incapable of hydrogen bonding on to adjacent chains.

(e) *Secondary Cellulose Acetates.*—When a primary acetate is hydrolysed, the increase in the intensity of the OH band relative to that of the CH bands is accompanied by a gradual shift in the OH frequency from 3480 to about 3490 cm.$^{-1}$. The shoulder at 3558 cm.$^{-1}$ is less marked in the spectra of the secondary acetates, as would be expected if this band is due to relatively unperturbed hydroxyl groups. The shift of the main OH absorption band to higher frequencies is probably to be explained by an increasing amount of inter-chain hydrogen bonding which may be weaker than the intra-chain bonding because of the steric effects of the acetyl groups. Such an explanation would be in accordance with the observed solubilities, triacetates being soluble in methylene chloride and the secondary acetates in acetone.

It has been shown that for primary acetates containing relatively few hydroxyl groups it is possible to detect non-uniformity of substitution by means of the contour of the OH absorption band. With secondary acetates the detection of small regions of non-uniformity is more difficult because the number of strongly bonded hydroxyl groups is a smaller proportion of the total number. However, by analogy with the cyanoethyl celluloses, measurement of the symmetry indices of the OH bands would be expected to give some information on the uniformity of substitution. Several secondary acetates with a degree of substitution between 2·4 and 2·5 have been studied. Some of these were soluble in dry acetone and some in aqueous acetone, and although the OH frequency varied little from 3490 cm.$^{-1}$ the symmetry index of those soluble in aqueous acetone was appreciably greater than the value of unity found for acetone-soluble derivatives. The spectrum of a typical acetone-soluble secondary cellulose acetate in the dried and in the undried state is shown in Fig. 2, No. 16, and, as with the primary acetates, graphical separation gives three bands due to absorbed water.

(f) *Cellulose Acetate Butyrates.*—In the undried state primary acetate butyrates show three OH bands at 3490, 3553, and 3631 cm.$^{-1}$, and in this respect are analogous to the primary cellulose acetates. However, the relative intensities of these three bands vary with the acetyl : butyryl ratio, the intensity of the 3490 cm.$^{-1}$ band increasing relatively to the intensities of the 3553 and 3631 cm.$^{-1}$ bands with increasing butyryl content. This intensity variation is in accordance with the decrease in water imbibition which accompanies an increase in the butyryl content. In the dry state the primary acetate butyrates show a single OH frequency at about 3486 cm.$^{-1}$ with a weak shoulder at about 3560 cm.$^{-1}$. As with the secondary cellulose acetates, the OH frequency of a secondary acetate butyrate is a few wave-numbers higher than that of the corresponding primary ester and is found at 3495 cm.$^{-1}$. The spectra of two primary acetate butyrates of high and low acetyl content are shown for dried and undried samples in Fig. 2, Nos. 17 and 18, and the spectrum of a secondary cellulose acetate butyrate is shown in Fig. 2, No. 19.

At low butyryl values the CH absorption of a cellulose acetate butyrate is similar to that of a cellulose acetate, but with increasing butyryl content several changes take place, *viz.*, (i) the 2956 cm.$^{-1}$ band splits into two components at 2944 and 2964 cm.$^{-1}$; (ii) the 2898 cm.$^{-1}$ band is shifted to 2881 cm.$^{-1}$; (iii) the intensity of the shoulder at about 3024 cm.$^{-1}$ is reduced.

(g) *Miscellaneous Cellulose Esters.*—The spectra of cellulose laurate, cellulose laurate naphthenate, and cellulose acetate stearate are all very similar in the 3-μ. region, and the presence of the large non-polar side chains reduces the water absorption to such an extent that no changes could be observed between the spectra of samples which had been subjected to intensive drying

and those which had been measured in moist air. The OH frequencies observed for highly substituted esters of this type are: cellulose laurate, 3476 cm.$^{-1}$, cellulose laurate naphthenate, 3480 cm.$^{-1}$, and cellulose acetate stearate, 3485 cm.$^{-1}$. The spectrum of cellulose laurate is illustrated in Fig. 2, No. 20. From the nature of the side chains and the fact that these esters are soluble in benzene it is unlikely that there is any inter-chain hydrogen bonding, so that any hydrogen bonding must be intra-chain in character, probably taking place between hydroxyl and carbonyl groups in the adjacent 2- and 3-positions. No evidence was found for relatively unperturbed hydroxyl groups in the spectra of any of these esters. This may be due to the effect of the large acyl radicals, substitution in the 6-position being easier than substitution in both the 2- and the 3-position. If this is so, then in a highly substituted ester there would be fewer OH groups in the 6-position than in the 2- and 3-positions, and because of the lower extinction coefficient of non-hydrogen bonded OH groups the detection of such groups would be difficult. It is of interest that the value of the OH frequency is affected to a slight extent by the nature of the acyl groups.

(h) *Quantitative Measurements on the Hydroxyl Absorption of Cellulose Acetates.*—As the intensity of the hydroxyl band is a function of the number of hydroxyl groups, it should be possible to devise a semi-empirical method for the determination of the degree of hydrolysis of a secondary cellulose acetate providing that the ester does not show any gross irregularities of

FIG. 3.

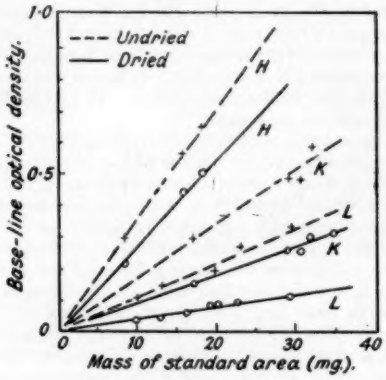
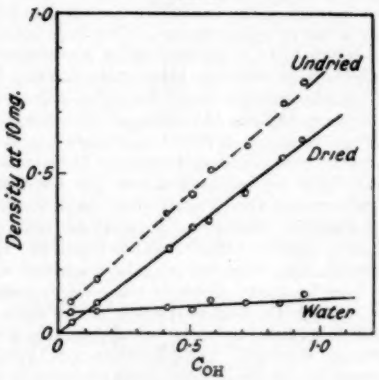


FIG. 4.



substitution. There are two ways in which such an analysis can be carried out in the 3-μ. region: in the first, the film thickness is eliminated by taking the ratio of the optical densities of the OH and one of the CH bands; in the second, the optical density of the OH band alone is measured together with the film thickness. Measurements are made for a number of cellulose acetates of known degrees of substitution and an empirical calibration curve is set up from which the hydroxyl content of any cellulose acetate can be read off. The difficulty in the first method lies in the elimination of scattering and reflection losses at the film surfaces. Although these losses can be reduced by mounting the film in Nujol, this masks the CH absorption. A good match for the refractive index of cellulose acetates can be obtained by a suitable mixture of carbon tetrachloride and carbon tetrabromide, both of which are transparent in the 3-μ. region. Both these substances, however, cause a limited swelling of cellulose esters, with consequent modification of the hydroxyl absorption. It is possible that a fluorocarbon could be used but this has not been tried. A further disadvantage of the method is that it could only be applied to simple esters, because with mixed esters the CH absorption varies with the relative amounts of the various acyl groups. In the second method the scattering and reflection losses may be eliminated by using a base-line optical density method. The simplest way of obtaining a measure of the film thickness is by cutting a standard area of film with a template and weighing it. Since the density of a cellulose ester is almost independent of the hydroxyl content, the mass of the standard area of the film may be used as a measure of the film thickness. The error introduced by day-to-day variations in the relative humidity of the atmosphere and the consequent variations in the moisture content and mass of the films will be small. To avoid

errors due to variations in the thickness of the films, a number of readings can be taken of the absorption at different parts of the film, and the resulting optical densities averaged. Alternatively, the film can be mounted off-focus so that the radiation passes through almost the entire sample. These two methods give the same results provided that the variations in thickness are small.

A number of measurements have been made of the base-line optical densities of the hydroxyl band for several cellulose acetate films of varying acyl content both in the dry state and at some constant relative humidity, namely, the relative humidity at the primary focus of the Grubb–Parsons S-3 spectrometer under standard operating conditions. The measurements were made by using the relatively low dispersion of a sodium chloride prism, and it was shown that the band area was the same linear function of the peak optical density both for dried and for undried samples, so that the difference between the measurements on undried and dried samples should be a measure of the water content. In Fig. 3 is plotted base-line optical density against the mass of a standard area of film for three cellulose acetate samples in the dried and in the undried state. In each case straight lines were obtained which passed through the origin. Similar measurements were carried out on a number of cellulose acetates and the results are summarized in Fig. 4 which shows a graph of base-line optical density at constant mass (10 mg.) against the hydroxyl content for a series of cellulose acetates (C_{OH} = 0·04—0·94) in the dried and in the undried condition. The difference between these two curves is also plotted and this, as explained above, must be related to the water absorption of the sample. One possible explanation of the shape of these curves is the following: if the curve for the optical density of undried samples is extrapolated to cut the optical density axis, the intercept may represent the non-bonded water in a cellulose triacetate. If the amount of non-bonded water is roughly independent of the degree of substitution, then the bonded water would be a linear function of the number of hydroxyl groups. No attempt has yet been made to correlate the water absorption band with the total amount of absorbed water.

The fact that the graph shown in Fig. 4 for dried cellulose acetates passes through the origin shows that there can be no appreciable contribution to the hydroxyl band from the first overtone of the stretching frequency of the ester carbonyl group.

Some measurements have also been made on the intensity of the hydroxyl absorption of cellulose acetate butyrates, and the results so far obtained show that, provided the measurements be carried out on dried samples, the calibration curves obtained for dried cellulose acetates can be used, *i.e.*, that the extinction coefficient of the OH absorption band in cellulose acetate butyrates is not very different from that in cellulose acetates. The results obtained in this way for a number of cellulose acetate butyrates agree with the chemical determinations of the hydroxyl content within the limits of error of the latter, but as this error is rather large this does not constitute a reliable test.

It is also possible to obtain calibration curves for the analysis of cellulose ethyl ethers, and there seems to be no reason why the method should not be perfectly general for cellulose derivatives.

The authors thank Mrs. J. M. Shreeve for her assistance in the experimental work, Dr. J. H. MacGregor for the samples of cyanoethyl cellulose, Mr. E. P. Sharman and Mr. J. P. Stoneman for the cellulose esters, Dr. R. D. Preston for the sample of *Valonia ventricosa*, and the Directors of Courtaulds Limited for permission to publish this work.

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352. *The Oxidation of Sulphurous Acid.*

By Henry Bassett and William G. Parker.

The oxidation of sulphurous acid by oxides of manganese, by ferric and cupric salts, and by molecular oxygen in presence of various dissolved salts has been studied with special reference to the proportions of sulphate and dithionate which are formed.

Oxidation by the solid oxides occurs on the surface and, while the proportion of dithionate formed is specific for each polymorph, it is independent of practically all other factors. Dithionate can only be formed when an oxide is reduced in one-electron steps. It can be formed with the oxides of manganese owing to the well-defined ter- and quadri-valent stages of the metal. It depends on surface adsorption of SO_3'' ions : either they are discharged successively in two single-electron steps to form sulphate or, alternatively, two of them after partial discharge unite to form S_2O_6''. The lattice structure of the individual oxide determines the extent to which these two modes of oxidation of the adsorbed SO_3'' will occur.

Ferric hydroxide dissolves before it is reduced by sulphurous acid, so that the mechanism is somewhat different in this case and involves a complex ferrisulphite anion. Oxidation of the sulphite to dithionate is almost quantitative, and the same applies to oxidation by ferric sulphate and ferric nitrate. Ferric chloride gives a much smaller proportion of dithionate, and very little in presence of hydrochloric acid, which is connected with the high stability of ferrichloride anions.

It seems clear that the oxidation of sulphurous acid by molecular oxygen follows a chain mechanism, but that which is usually accepted (due to Franck and Haber, *Sitzungsber. Preuss. Akad. Wiss. Berlin*, 1931, 250) is inadequate to explain the variety of effects observed when this oxidation occurs in presence of salts. The Franck–Haber chain mechanism for the uncatalysed oxidation can be improved by assuming that the oxygen reacts in the form of ionic complexes such as $[O_2 \rightarrow SO_3]''$ and $[O_2 \rightarrow S_2O_3]''$.

The enormously accelerated oxidation caused by manganese ions is attributed to the formation of complex sulphite ions carrying co-ordinated oxygen molecules such as $[O_2 \rightarrow Mn(SO_3)_2]''$ which rapidly undergo self-oxidation and -reduction. Cobalt, nickel, and ferrous iron can give rise to similar but less active complexes.

Assumption of these two types of oxygen addition complexes enables satisfactory explanations to be given of all the peculiar results obtained when sulphurous acid is oxidised by molecular oxygen in presence of salts.

Concentrated sulphurous acid solution was oxidised in three different ways, and the work is presented accordingly in three parts as follows :

1. Oxidation by oxides of manganese.
2. Oxidation by ferric and cupric salts.
3. Oxidation by free oxygen in the presence of dissolved salts.

Dithionic acid as well as sulphuric acid may be formed in the oxidation of sulphurous acid by air and other oxidising agents. Dithionic acid, which is very stable towards oxidation, is an individual product and not an intermediate stage in the formation of sulphuric acid. It follows therefore that these two acids are derived from sulphurous acid by independent reactions, and the principal object of this work was to examine the change in the relative quantities of sulphate and dithionate formed by each oxidation in an attempt to determine the mechanisms of these reactions. The work is a continuation of that by Bassett and Henry (*J.*, 1935, 914).

Concentrated sulphurous acid solutions were used throughout, partly because they were relatively reproducible and easily prepared by saturating the aqueous solutions with sulphur dioxide at the temperature of the experiment, and partly because such solutions were needed to reduce some of the natural oxides sufficiently rapidly (Part 1) and to obtain a reasonable proportion of dithionate in the uncatalysed oxidation by molecular oxygen (Part 3).

1. Oxidation by the Oxides of Manganese.

Review of the Literature.—Dithionic acid was first prepared by Gay-Lussac and Welter (*Ann. Chim. Phys.*, 1819, **10**, 312) who passed sulphur dioxide through water containing manganese dioxide in suspension. Heeren (*Pogg. Annalen*, 1826, **7**, 55), by the same method and using finely ground " grau Braunstein " (*i.e.*, pyrolusite, MnO_2), found that some sulphate was always formed, in amount varying from 0·370 to 0·135 part of H_2SO_4 to 1 part of $H_2S_2O_6$. Berzelius (" Lehrbuch," Dresden, 1825, Vol. II, p. 467), without giving experimental evidence, attributed the sulphate formation to " oxyd-hydrat " (*i.e.*, Mn_2O_3,H_2O) which he considered was always present as impurity in the pyrolusite. He thought that pure manganese dioxide gave only dithionate. Heeren tested this point by determining the weight of oxide dissolved, as well as the amounts of sulphate and dithionate formed. The weight of oxide dissolved was always considerably less than that required by Berzelius's theory, so Heeren concluded that some of the sulphate must have been formed by oxidation by MnO_2, the equivalent weight of which is much less than that of the requisite amount of Mn_2O_3,H_2O.

Heeren also examined the action of sulphurous acid on finely ground " glanz-Braunstein " (*i.e.*, manganite, natural Mn_2O_3,H_2O) and on a freshly precipitated " oxyd-hydrat " purified by means of very dilute nitric acid. The action on the mineral was very slow but in the case of the precipitated oxide some dithionate was formed. He attributed the varying proportions of dithionate to sulphate obtained in his experiments to three factors: (1) temperature—high temperatures caused high yields of sulphate by decomposition of dithionate; (2) presence in the dioxide of Mn_2O_3,H_2O which gave more sulphate than dithionate; and (3) state of division of the oxide—the finer the oxide the greater the yield of dithionate. Spring and Bourgeois (*Bull. Soc. chim.*, 1886, **46**, 151; Spring, " Collected Researches," p. 1123), from experiments with powdered pyrolusite and with freshly precipitated oxides, came to exactly the opposite conclusion as to the influence of the state of division.

All this earlier work suffers from two defects: (*a*) no analyses, and in particular no determinations of the available oxygen, appear to have been made of either the natural or the artificially prepared oxides which were used in the experiments; and (*b*) the marked effect of manganese salts in catalysing oxidation of sulphurous acid by molecular oxygen was probably not known or appreciated and was neither guarded against nor allowed for.

The formation of a red solution when sulphur dioxide is passed into a suspension of ferric hydroxide was first noticed by Berthier (*Ann. Chim. Phys.*, 1843, **7**, 78) and the presence of ferric sulphite in this solution was confirmed by Seubert and Elten (*Z. anorg. Chem.*, 1893, **4**, 86). The red solution becomes pale green when kept, and ferrous sulphite and dithionate are formed (Gélis, *Bull. Soc. chim.*, 1863, **5**, 333; *Ann. Chim. Phys*, 1862, **65**, 222). J. Meyer (*Ber.*, 1901, **34**, 3606) assumed that the course of the reaction with manganese dioxide was similar, *viz.*: $2MnO_2 + 3H_2SO_3 = Mn_2(SO_3)_3 + 3H_2O + O$; $Mn_2(SO_3)_3 = MnSO_3 + MnS_2O_6$; $MnSO_3 + O = MnSO_4$. Carpenter (*J.*, 1902, **81**, 1) endeavoured to trace a connection between the yields of dithionate obtained from hydroxides of the iron group and their heats of reduction.

Several early workers observed that no dithionate was formed when the peroxide of lead, barium, magnesium, or sodium reacted with sulphurous acid. Luigi Marino (*Z. anorg. Chem.*, 1907, **56**, 233) confirmed this for the peroxides of lead and barium whereas with pure MnO_2 he obtained dithionate plus a little sulphate which he supposed was formed by an " induced " reaction: $MnO_2 + 2SO_2 = MnS_2O_6$ (main reaction); $MnS_2O_6 + MnO_2 = 2MnSO_4$ (" induced " reaction). The differing behaviour of the peroxides was ascribed to differences in their constitution.

After this date little work has been recorded on the reaction of oxides of manganese with sulphurous acid but some important work has been done on their constitution.

It is necessary to consider what is known about the structures of the oxides of ter- and quadri-valent manganese before the oxidation of sulphurous acid by these compounds can be profitably discussed.

The Natural Oxides.—A study, with *X*-ray examination, of manganese oxide minerals has been published by Fleischer and Richmond (*Econ. Geology*, 1943, **38**, 269).

Pyrolusite, MnO_2, crystallises in the tetragonal system with the rutile type of structure (Ferrari, *Atti R. Accad. Lincei*, 1926, **3**, 224). There is always a slight deficiency of oxygen. The manganese is quadrivalent.

Ramsdellite is an orthorhombic form of MnO_2, first described by Ramsdell (*Amer. Min.*, 1932, **17**, 143; see also Fleischer and Richmond, *loc. cit.*).

Manganite, Mn_2O_3,H_2O, is monoclinic and belongs to the boehmite–lepidocrocite group. The arrangement of the manganese atoms in the crystal suggests equal valencies of three. More value must be attached to this result than to the suggestion of a mixed two and four valency given by the behaviour of the compound with acids, though this view of its structure is supported by Krishnan and Banerjee (*Trans. Faraday Soc.*, 1939, **35**, 385).

Hausmannite is tetragonal and a pseudo-spinel. Chemical and electrochemical behaviour support the view that the manganese is bi- and ter-valent (MnO,Mn_2O_3) rather than bi- and quadri-valent.

Braunite occurs massive and also as dark brownish-black or steel-grey crystals. Combined silica is probably always present and on account of this the accepted formula for the mineral is $3Mn_2O_3,MnSiO_3$.

Oxides of Manganese prepared artificially.—Great care must be taken in drawing conclusions as to the structures of the oxides of manganese either from oxygen-pressure curves or from *X*-ray diagrams. Drucker and Huttner (*Z. physikal. Chem.*, 1928, **131**, *A*, 237) showed that the oxygen-pressure curves varied within certain limits with the physical condition of the oxide. Oxides prepared in a dry way are usually well crystallised, while those obtained by a wet method are amorphous or poorly crystalline. Le Blanc and Wehner (*Z. physikal. Chem.*, 1934, **168**, *A*, 67) found that the MnO structure persisted up to $MnO_{1\cdot13}$, that of Mn_3O_4 up to $MnO_{1\cdot42}$, and that of Mn_2O_3 up to $MnO_{1\cdot18}$, and this complicates the interpretation of powder diagrams. MnO_2, however, though normally slightly deficient in oxygen, cannot lose more without the appearance of the Mn_2O_3 lattice. Dubois (*Compt. rend.*, 1934, **199**, 1416; 1935, **200**, 1107) established the existence of at least two polymorphs of MnO_2 and of Mn_2O_3. The oxide obtained by heating manganese nitrate gave an *X*-ray diagram identical with that of pyrolusite, and this oxide he called β-MnO_2. The oxides formed by spontaneous decomposition of $HMnO_4$ and by reduction of permanganate solution with manganese sulphate gave, after repeated washing with hot nitric acid, $MnO_2,0{\cdot}88H_2O$ and $MnO_2,1{\cdot}66H_2O$ respectively. They had identical *X*-ray diagrams, quite different from that of pyrolusite. Dubois called this α-MnO_2. Evidence for a third polymorph was also given but was not conclusive. Glemser (*Ber.*, 1939, **72**, 1879) obtained $MnO_{1\cdot97}$ by wet methods very similar to those used by Dubois (*loc. cit.*), which may be correlated with Dubois's α-MnO_2 although Glemser called it γ-MnO_2 and said that its *X*-ray diagram was not identical with that given by Dubois for his α-MnO_2.

α-MnO_2 is reduced by hydrogen to Mn_2O_3 at 170°, and the β-MnO_2 at 220°. The Mn_2O_3 is further reduced at 260° (Dunoyer, *Compt. rend.*, 1939, **208**, 1018). Both α- and β-MnO_2 above 600° in oxygen or nitrogen yield β-Mn_2O_3 (see below). Dehydration in air of the dimanganese trioxide prepared by oxidation of manganese sulphate with hydrogen peroxide in alkaline solution (Carnot, *Compt. rend.*, 1888, **107**, 999, 1150) is accompanied by some oxidation. Above 600° a form of Mn_2O_3 is obtained, giving very clear *X*-ray pictures, which Dubois (*loc. cit.*) called β-Mn_2O_3.

The initial precipitate obtained by the hydrogen peroxide method looks amorphous but gives a good *X*-ray diagram identical with that of manganite. On exposure to air at room temperature the precipitate loses water slowly and approaches the composition required by Mn_2O_3,H_2O. When this material is heated to 100° *in vacuo*, this composition is passed through as a definite stage, but more water is easily lost below 250°, or even a little above 100°, to give Mn_2O_3 without any dioxide. Dubois called this variety of the oxide α-Mn_2O_3 as it is quite different from the β-Mn_2O_3 obtained at 600° and into which it passes on heating to this temperature.

Mn_3O_4 has not been prepared in a pure state by a wet method. Thermal decomposition of the higher oxide, nitrate, carbonate, or oxalate at appropriate temperatures yields crystalline products having the same composition and *X*-ray structure as hausmannite.

Dubois's β-Mn_2O_3 and bixbyite, $(Mn,Fe)_2O_3$, are isometric and have the *C*-structure typical of certain sesquioxides (Zachariasen, *Norsk Geol. Tidskr.*, 1927, **9**, 310). All the manganese in bixbyite, and therefore in β-Mn_2O_3, is six-co-ordinated and tervalent.

Braunite is tetragonal, although Le Blanc and Wehner (*loc. cit.*) stated that bixbyite from Dugdale Range, Utah, and braunite from Oehrenstock near Ilmenau gave identical *X*-ray diagrams.

Verwey and De Boer (*Rec. Trav. chim.*, 1936, **58**, 531) have shown that Dubois's α-Mn_2O_3 has the hausmannite structure with vacant lattice positions. It is related to hausmannite as γ-Fe_2O_3 is to Fe_3O_4 and would be expected therefore to contain only tervalent manganese. In spite of this Verwey and De Boer suggest that hausmannite is $Mn^{II}_2Mn^{IV}O_4$ because of its electrical conductivity rather than $Mn^{II}Mn^{III}_2O_4$.

There seems to be little doubt from the *X*-ray work carried out on the compounds that

braunite is structurally much more closely related to bixbyite and β-Mn_2O_3 than to hausmannite and α-Mn_2O_3. The part played by the silica in braunite is still obscure. It would be possible, if conditions were otherwise suitable, for a Mn^{III} atom in a compound ($Mn^{III}_2O_3$) to be replaced by a silicon atom if at the same time another Mn^{III} atom were replaced by Mn^{II}. Now, in the *C*-type oxide structure to which bixbyite and β-Mn_2O_3 belong, all the metal ions are six-co-ordinated. In silicon–oxygen structures the silicon is normally in four co-ordination, but it can enter into six co-ordination as in the fluorosilicates. It seems possible that braunite may be derived in this manner from β-Mn_2O_3, but that some distortion of the lattice is caused and a limit set to the extent of the replacement of manganese by silicon (*a*) by the unusual co-ordination of the silicon and (*b*) by the fact that the ionic character of the silicon–oxygen links is rather low for a structure which is essentially ionic. It is not easy to say whether the accepted formula for braunite, $3Mn_2O_3.MnSiO_3$, is exact or only approximate.

The number of polymorphs of MnO_2 and Mn_2O_3 which exist still appears to be somewhat uncertain while views still differ as to their structures (Fleischer and Richmond, *loc. cit.*; Imperial Institute Ann. Report, 1946, p. 31; Fyfe, *Nature*, 1949, **164**, 790; see also *Ann. Reports*, 1949, **46**, 73).

An unfortunate complication has been introduced into the nomenclature of the polymorphs. It has arisen from the recognition that Dubois's low-temperature or α-form of Mn_2O_3 is related to the pseudo-spinel hausmannite, Mn_3O_4, in the same way that γ-Fe_2O_3 is related to the spinel Fe_3O_4. Its structure does appear to be fundamentally similar to that of γ-Fe_2O_3 and γ-Al_2O_3 although probably tetragonal rather than cubic (Le Blanc and Wehner, *loc. cit.*). Dubois's α-Mn_2O_3 is now sometimes called γ-Mn_2O_3 for this reason and this has led to his β-Mn_2O_3 being called α-Mn_2O_3 which is unsatisfactory since it is body-centred cubic and does not correspond to α-Fe_2O_3 or α-Al_2O_3 which are hexagonal. It would appear better, on the whole, to retain Dubois's original nomenclature for the forms of Mn_2O_3 and this has been done in the present paper. The case illustrates the great difficulty in finding a satisfactory nomenclature for polymorphs.

Experimental.

Oxides of Manganese used in the Present Investigation. See Table II.—*Manganese dioxide.* (1) Pyrolusite, purchased, source unknown.

(2) Pyrolusite, purchased as manganite from Nova Scotia but found to be pyrolusite of high purity.

(3) Pyrolusite of good commercial grade, supplied as small pellets.

(4)(*a*) Manganese nitrate was heated to about 200°. The oxide produced was treated with concentrated nitric acid, washed, and dried for 3 hours at 100°. (*b*) Manganese nitrate (AnalaR standard) was heated to 154° under reduced pressure (20 mm. of Hg.) The oxide was washed free from nitrate and dried for 3 hours at 100°. This method (Krull, *Chemie der Erde*, 1932, **7**, 473) gives a minutely crystalline form of manganese dioxide.

(5)(*a*) and (*b*). Two preparations by the same method. Powdered potassium permanganate was slowly added to well stirred concentrated nitric acid at 0°. Stirring was discontinued after 3 hours but the mixture was kept for 2 days before collection of the oxide on a sintered glass funnel. This was a black, finely divided, product which filtered easily. It was used in the wet state and also after being dried at 96° for 3 hours.

(6) Manganese chloride solution was added to an excess of sodium carbonate solution, and chlorine bubbled through the mixture. The manganese dioxide formed was filtered off, washed, treated with dilute nitric acid, and again washed. It was used in the wet state and also after being dried at 96° for 3 hours.

(7) A 0·5M-solution of manganous sulphate, about 0·1N. with sulphuric acid, was electrolysed at 70°, at platinum electrodes (van Arsdale and Maier, *Trans. Amer. Electrochem. Soc.*, 1918, **33**, 109). The anode was a fine gauze, 4 sq. in. in area; a current of 0·4 amp. at 4 volts was used. After 10 hours a good yield of oxide had formed on the anode as a dense lustrous black film.

(8) Purchased precipitated MnO_2 of " AnalaR " quality.

Dimanganese trioxide. (9)(*a*) Manganite from Ihlefeld, Harz Mountains, one of the type localities for this mineral. This was a glistening black crystalline mineral, which on being ground gave a chocolate-brown powder. (*b*) Some of the same manganite was heated in air for an hour at 600°.

(10) Braunite from Ilmenau, Thuringia. This was a steel-grey crystalline mass containing patches of quartz. The combined silica content (9·5%) agreed very closely with that required for $3Mn_2O_3.MnSiO_3$ and so did the available oxygen.

(11) Manganese dioxide prepared as in 4(*b*) was heated at 550° in a slow current of oxygen for 4 hours. There was no change in the appearance of the oxide.

(12) Preparation (8) was heated at 900° in an air current for 3 hours. The oxide lost 12·6% in weight but there was no change in colour.

(13) 50 C.c. of 0·2N-ammonia were added in the cold with stirring to a mixture of $MnSO_4.4H_2O$ (2 g.) in water (350 c.c.) and 2N-hydrogen peroxide (100 c.c.). The mixture was heated rapidly to the b. p. and kept there for 4 minutes. The oxide filtered satisfactorily and was washed and then dried *in vacuo* at 100°.

Trimanganese tetroxide. (14) Hausmannite from Bigrigg, Cumberland. The steel-grey crystals gave a reddish-brown powder on being ground.

(15) Ground pyrolusite [sample (2)] was heated to 950—1000° for 3 hours in a slow air current. There was no change in appearance.

(16) Manganese dioxide, prepared as in 4(*b*), was heated to 950—1000° for 2 hours in a slow current of air. The oxide lost 14·9% in weight and became reddish-brown.

(17) Manganese dioxide, prepared as in (6), was heated to 200° in a slow current of hydrogen. The oxide was rapidly reduced to a greenish product.

Analysis of Oxides of Manganese.—The manganese content was determined by the phosphate method. The available oxygen was determined in two ways : (*a*) by Bunsen's method in an all-glass apparatus through which a stream of carbon dioxide carried the chlorine evolved into cold acidified potassium iodide solution; and (*b*) dissolving the oxide in excess of standardised sodium oxalate solution acidified with sulphuric acid, and back-titration with standard permanganate (Lunge, "Sulphuric Acid and Alkali," 2nd edn., 1896, Vol. III, p. 274). Bunsen's method generally gave somewhat lower values for the available oxygen than did Lunge's method and this was traced to oxidation of oxalate by atmospheric oxygen catalysed by the manganese salt. The following results illustrate this effect.

Experimental conditions.	Titre (c.c.) with 0·1N-$KMnO_4$.
Acidified sodium oxalate (25 c.c.) was heated to 60° and titrated immediately.....	28·6
The oxalate solution, plus manganese sulphate (0·3 g.), was heated to 95° and titrated immediately	28·6
As in the preceding case but kept at 80—90° for 2 hours and then titrated.....	27·5
As in the preceding case but in an atmosphere of CO_2.....	28·6
Two estimations of some pyrolusite made by dissolving the mineral as rapidly as possible in sodium oxalate solution at 60° gave 0·99 and 0·98 atom-equiv. of available oxygen respectively.	
Two estimations of the same pyrolusite by sodium oxalate in an atmosphere of CO_2 gave 0·97 atom-equiv. of available oxygen in both cases.	
Analysis of the same pyrolusite by the Bunsen method gave 0·94 atom-equiv. of available oxygen.	

Hot acidified sodium oxalate alone is not oxidised by air, even on fairly long exposure, but the presence of manganese sulphate catalyses the oxidation. The precipitated dioxides which dissolved readily, and in most cases in the cold, and the pyrolusite which was estimated in an atmosphere of carbon dioxide, gave values which were consistently 3% higher than the corersponding values obtained by the Bunsen method. Under the conditions of the analyses it was estimated that dissolved oxygen could lead to an error of 2·7% and this appears to provide a reasonable explanation of the discrepancy between the two methods.

Clearly, estimation by the sodium oxalate method of the available oxygen in manganese oxides is valueless unless it is made in an oxygen-free atmosphere and with sodium oxalate solution prepared with well-boiled water. Only results obtained by Bunsen's method are given in Table II.

Bhatnagar and his co-workers (*J.*, 1939, 1441) obtained good agreement between the two methods but no details of the procedures or of any precautions were stated. Schroder (*Z. off. Chem.*, 1910, **16**, 270) studied Lunge's method for the estimation of available oxygen in pyrolusite. His results were high and he showed that even the titration of oxalic acid with potassium permanganate suffered a small error owing to induced atmospheric oxidation when the titration was slow (5—10 minutes), and the error was greatly increased by the presence of manganese salts, even in strongly acid solution titrated rapidly.

Before examining the oxidation of sulphurous acid by the various oxides of manganese it was necessary to determine the constancy of the results for any one oxide.

Effect of concentration. The effect of variation in concentration of the sulphurous acid, on the proportion of dithionate to sulphate in the oxidation products, was found to be negligible over a wide range for concentrated solutions but in dilute solutions the proportion of dithionate formed appears to be lower (Table Ia).

Effect of temperature. The solubility of sulphur dioxide in water was found by Freese (*Chem. Ztg.*, 1920, **44**, 294) to be 228·3 g./l. at 0°, 94·1 at 25°, and 54·1 at 40°. The concentration of the saturated solutions does not fall below 1·7N. even at 40°, and such a change would not influence the products of oxidation. Furthermore Spring and Bourgeois (*loc. cit.*) showed that dithionic acid is not rapidly decomposed below 75°. It could reasonably be assumed that, unless the mechanism of the oxidation was affected by temperature, close temperature control of the solutions was unnecessary. This was borne out by experiment (Table Ib).

Particle size was also found to be without influence on the yield of dithionate (Table Ic).

TABLE I.

(*a*) *Effect of concentration of* H_2SO_3 *solution at* 25°.

Prep. no. (see Table II).	Normality of H_2SO_3 solution.	Yield of dithionate, %.	Prep. no. (see Table II).	Normality of H_2SO_3 solution.	Yield of dithionate, %.
1 (Pyrolusite) ...	3	96	8 (Precipitated MnO_2)	3	77
,, ...	2	95	,,	0·01	64
,,	1	96			

(*b*) *Effect of temperature.*

Prep. no. (see Table II).	Temp. of saturated H_2SO_3 solution.	Yield of dithionate, %.
5(*b*) (Precipitated oxide in wet state) ...	0°	38
,, ,, ,, ,, ...	25	36
,, ,, ,, ,, ...	40	36

(*c*) *Effect of mechanical grinding on the behaviour of an oxide.*

Treatment of pyrolusite No. 3 (see p. 1543).	Time to dissolve similar quantities in saturated H_2SO_3 solution.	Yield of dithionate, %.
(1) Pellets rough ground in a porcelain mortar	60 hr. (approx.)	96
(2) Ground oxide from (1) was ground wet for an hour in an agate mortar	24 ,,	96
(3) Pellets ground in a ball mill (work kindly arranged by Dr. Taylor of I.C.I., Ltd., Billingham). This material was at least twice as fine as the agate-ground material ...	6 ,,	96

The results of these preliminary experiments show that the behaviour of an oxide is not determined by the changes in the conditions described. Anomalies recorded by earlier workers were most probably caused by the method used. No mention is made of the use of an inert atmosphere and it may be assumed that the solutions were in contact with air for widely varying times—evidently the strongly catalytic effect of manganous salts on the oxidation of H_2SO_3 by air was not considered. The magnitude of this effect in the production of sulphate, and sulphate only, is shown in Part 3 of this work and again in Table II of the present Part, where the amount of air-oxidation is calculated for each of the oxide reactions. These reactions did not take place in contact with air, although all trace of air was not rigidly excluded. Moreover, the speed of the catalysed reaction increases with rise of temperature. If allowance is made for this additional reaction, the results of Heeren and others may be explained. For example, Heeren obtained less sulphate when the oxide was more finely divided because it reacted in a shorter time and was accompanied by less air-oxidation. Again, the sulphate yield at higher temperatures was always higher because the rate of the subsidiary reaction had greatly increased. Spring and Bourgeois recorded two experiments with sulphurous acid solution at 21—22°, in which finely ground pyrolusite produced more sulphate than coarse lumps of the same mineral. This result can only be explained if it is assumed that in the experiment with the fine material the solution was in contact with the air for a longer period than in the other case.

The following procedure was adopted for all the oxides investigated by us. 80 C.c. of distilled water were saturated with sulphur dioxide at room temperature in a 160-c.c. Dreschel bottle and 0·2—0·4 g. of the oxide was added. The bottle was closed and shaken at intervals until the oxide had dissolved. The bottle was cooled in water in those cases where dissolution of the oxide occurred rapidly, to prevent any large rise of temperature. Sufficient hydrochloric acid was then added to decompose any manganese sulphite and a current of carbon dioxide was passed through the solution until no trace of sulphur dioxide remained, a final test being made with iodine and starch paste. After dilution to 200 c.c., manganese, sulphate, and dithionate were determined in separate portions, the dithionate after removal of the sulphate, and manganese with barium hydroxide. Details are given in Part 3.

To calculate the proportion of sulphur dioxide oxidised to dithionate by the oxide, the amount of dithionate formed and the manganese content of the solution alone were used. The results of the catalysed reactions described in Part 3 indicate clearly that oxidation of sulphurous acid solution by free oxygen in the presence of manganese salts gives sulphate only and that the quantity of dithionate formed is negligible. The dithionate found in the analysis must therefore arise entirely by oxidation by the manganese oxide, and the amount of oxygen required could be calculated and deducted from the amount of oxygen known to be available from the manganese content of the solution and the analysis of the oxide already made. The sulphate formed was calculated from the remainder of the available oxygen. In this way the sulphate arising from oxidation by dissolved air and any air contained in the space above the solution was not included.

It is now possible to consider the oxidation of sulphurous acid by various oxides of manganese. Analysis of these oxides, whether natural or artificially prepared, showed that none of them corresponded exactly to the nominal compounds MnO_2, Mn_2O_3, or Mn_3O_4. The discrepancy was particularly marked

with manganese dioxides. The best pyrolusite sample was $MnO_{1.94}$, and an oxide formed by thermal decomposition of manganese nitrate had a similar proportion of available oxygen. Precipitated oxides,

TABLE II.

Oxidation of sulphurous acid by the oxides of manganese. Proportion of dithionate formed.

No. of prep. (p. 1543).	MnO_x: value of x, Bunsen method.	Probable nature of oxide.	Mn content of the solution as $NH_4MnPO_4.H_2O$, g.	$BaSO_4$ (g.) from S_2O_6''. Oxidation by the oxide.	$BaSO_4$ (g.) from SO_4''. Oxidation by the oxide.	$BaSO_4$ (g.) from air-oxidation.	SO_2 (%) oxidised to S_2O_6'' by oxide.
A. Manganese dioxides.							
1	1·92	MnO_2	0·1227	0·2731	0·0065	0·0096	97·7
2	1·94	MnO_2	0·1068	0·1204	0·0056	0·0069	95·6
4(*a*)	1·93	MnO_2	0·2544	0·5506	0·0217	0·0308	92·2
4(*b*)	1·84	MnO_2	0·0793	0·1519	0·0078	0·0080	95·1
5(*a*) (1) Wet	1·87	Amorphous	0·895	0·303	0·813	0·077	27·2
5(*a*) (2) Dried	,,	MnO_2	1·331	1·826	0·520	0·125	77·8
5(*b*) (1) Wet	1·85	Amorphous	0·1950	0·0898	0·1626	0·0313	35·6
5(*b*) (2) Dried	,,	MnO_2	0·0838	0·1041	0·0372	0·0504	73·7
6(1) Dried	1·76	Mixture of MnO_2 and amorphous	0·1280	0·1083	0·0621	0·0242	63·6
6(2) Dried	1·76	MnO_2	0·2104	0·2399	0·0808	0·0650	74·8
7	1·95	MnO_2	0·2446	0·3834	0·1000	0·0142	79·3
8	1·91	MnO_2	0·3482	0·4947	0·1505	0·0415	76·7
B. Dimanganese trioxides							
9(*a*)	1·53	Manganite	0·1901	0·1189	0·0666	0·0074	64·1
9(*b*)	1·51	β-Mn_2O_3	0·1242	0·1382	0·0103	0·0501	93·1
10	1·42	Braunite	0·3243	0·2858	0·0282	0·1155	91·0
11	1·51	β-Mn_2O_3	0·2034	0·2340	0·0137	0·0108	94·5
12	1·42	Mixture of β-Mn_2O_3 and Mn_3O_4	0·2468	0·1894	0·0398	0·0040	82·6
13(1) Before drying	1·41	Manganite structure	0·3693	0·1670	0·1085	0·0235	60·6
13(2) After drying	1·41	α-Mn_2O_3	0·2511	0·1832	0·0390	0·0111	82·5
C. Trimanganese tetroxides.							
14	1·32	Hausmannite structure	0·3224	0·1674	0·0467	0·0420	78·2
15	1·36	,,	0·2319	0·1523	0·0363	0·1050	80·7
16	1·34	,,	0·2463	0·1218	0·0441	0·0159	73·4
17	1·18	,,	0·2638	0·0620	0·0183	0·0043	77·2

with the exception of an electrolytic preparation, gave lower values for the oxygen content. Treatment of an oxide with hot nitric acid increased the proportion of oxygen in the compound, and according to the literature many repetitions of this treatment will give ultimately $MnO_{2.0}$.

Discussion.—While the results (Table II) show that all the oxides do not produce the same proportion of dithionate in this reaction, it is possible to group the oxides according to their dithionate yields.

The manganese dioxides form three groups according to the dithionate yield, *viz.*: (1) 95—97%: pyrolusites and oxide produced by thermal decomposition of manganese nitrate; these belong to Dubois's β-MnO_2 group. (2) 74—79%: oxides prepared by a wet method and dried at a moderate temperature (96°), together with an oxide prepared electrolytically: this is probably α-MnO_2, as are the other members of this set. (3) Low and variable percentages: oxides freshly precipitated and used immediately in the wet state. These oxides are probably amorphous or only partly crystalline at this stage, and the amount of dithionate varies according to the extent to which crystal formation has occurred. Dissolution of these oxides was extremely rapid and may have taken place before reduction, so that the reaction was perhaps not entirely a surface reaction.

The dimanganese trioxides also form three groups, *viz.*: (1) 91—95%: braunite and oxides formed from the dioxide or manganite at approx. 600°. (2) 60—64%: manganite and one

precipitated oxide [No. 13 (1) in Table II]. (3) 82—83% : two oxides, one formed by precipitation and the other by heating a dioxide in air at 900° [No. 13 (2) and No. 12 respectively in Table II]. No. 13 (2) had lost nearly all its water and should therefore have been mainly α-Mn_2O_3. No. 12 was probably a mixture of β-Mn_2O_3 and Mn_3O_4, since α-Mn_2O_3 is not stable at 900°.

The trimanganese tetroxides form a single group, and this is in agreement with theory since only one form of the oxide is known. The yield of dithionate from this oxide, approximately 80%, is close to the yield from α-Mn_2O_3.

All these groups appear to be well defined, having regard to the limits of accuracy of the dithionate determination and the nature of the oxides. Any explanation of the mechanism of the oxidation must be compatible with them.

Sulphurous acid solution may be assumed to contain SO_2, SO_3'', S_2O_5'', H_2SO_3, $H_2S_2O_5$, HS_2O_5', and HSO_3' in amounts depending on the acidity and the total SO_2 concentration. Of these, SO_2, HSO_3' and SO_5'' have been identified by spectroscopy (Albu and Goldfinger, *Z. physikal. Chem.*, 1932, **16**, *B*, 338). In the oxidation of the solution by manganese dioxide, if the reduction $Mn^{4+} \longrightarrow Mn^{3+}$ occurred in a single step through the discharge of the doubly charged anions SO_3'' and S_2O_5'', the resulting neutral molecules would immediately react with water to form H_2SO_4 and $H_2S_2O_6$ respectively. The quantity of dithionate produced in this way is probably negligible since the concentration of S_2O_5'' ions is relatively small, and in the analogous reaction with PbO_2, which must occur in a single stage involving two electrons, very little dithionate is formed. It was suggested therefore by Bassett and Henry (*J.*, 1935, 914) that the large yield of dithionate in the oxidation by MnO_2 might be caused by reduction occurring in two steps through the well-defined tervalent state of manganese. Thus, in either the first step $Mn^{4+} \longrightarrow Mn^{3+}$ or the second step $Mn^{3+} \longrightarrow Mn^{2+}$, a single electron would be absorbed from a SO_3'' ion which could then lose its second electron, giving sulphate as before, or combine with another singly charged SO_3' ion to give S_2O_6''. Similarly, in a process which involves one electron at a time, HSO_3' ions may be discharged and a molecule of dithionic acid formed by two such neutral radicals.

It has been shown (Table II) that the reduction of tervalent manganese does result in large amounts of dithionate. The *X*-ray evidence shows that the whole of the manganese in manganite and the two forms of Mn_2O_3 is tervalent. Had such high yields not occurred it would be impossible to explain a 95% formation of dithionate in the reduction of MnO_2 by this two-step theory.

Since the proportion of dithionate is nearly independent of conditions, the possibility of complex formation must be examined. The formation of a complex when freshly precipitated ferric hydroxide reacts with sulphurous acid has been established (Seubert and Elten, and Gelis, *loc. cit.*). The first product is a reddish solution of complex ferric sulphite which slowly decomposes with a nearly quantitative yield of dithionate and only a very small amount of sulphate. Manganese could readily form anionic complex sulphites, *viz.*, $[Mn(SO_3)_3]^{3-}$ or $^{3-}$, and since this metal, like iron, is easily reducible to a lower valency stage the complexes could undergo self-oxidation and -reduction to either dithionate or sulphate. This explanation does not require that the proportions of dithionate formed by quadrivalent and tervalent manganese should have a predetermined relationship, but if such complexes are formed *in solution* before reduction occurs it does require that all oxides of one class (*e.g.*, dioxides) should produce the same proportion of dithionate. This is not the case, and therefore it is concluded that the oxidation of sulphurous acid by the oxides and hydroxides examined in this work occurs, not in solution, but on the surface of the oxide. Ferric hydroxide is an exception, dissolution occurring before reduction in that case. The pattern of the surface adsorption may be expected to be determined in large measure by the crystal lattice of the oxide but to be largely independent of the concentration of the solution. This would account for the fact that the proportion of dithionate formed in the reaction is the same over a wide range of concentration for any one variety of oxide.

Reaction on the surface probably has the general mechanism outlined above. An SO_3'' ion, for example, reacting at the surface of manganese dioxide, may be discharged in a single- or a two-step operation and the resultant neutral molecule may form sulphate, or the ion may be partly discharged and be at the same time in close proximity to another ion in a similar state so that the two link up to form a doubly charged S_2O_6'' ion. If this explanation is accepted it is reasonable to suppose that the products will depend largely on the structure of the oxides and the location of the reactive centres. The theory receives strong support from the results which are set out in Table II, for it certainly appears that the dithionate yields from the various

oxides fall into groups which can be correlated with the several polymorphic forms of the oxides. It might be supposed that the two polymorphic forms of Mn_2O_3 were respectively $Mn^{III}{}_2O_3$ and $Mn^{II}O,Mn^{IV}O_2$, that they dissolved and formed anionic complexes before reduction, and that these complexes contained Mn^{III} in the one case and Mn^{IV} in the other. The different yields of dithionate could then be ascribed to this difference. It would not be possible on this basis to account for manganite giving still a different proportion of dithionate, for this must yield the same solution as one or the other form of Mn_2O_3.

If the differences are determined by the crystal lattices this difficulty does not arise, for Mn_2O_3,H_2O would naturally have a lattice differing from those of α- and β-Mn_2O_3. It is clear from the *X*-ray evidence in any case that all the manganese in both forms of Mn_2O_3 and in manganite is tervalent.

A surface reaction seems to provide the only mechanism which can explain the different yields of dithionate from the two forms of crystalline MnO_2 and Mn_2O_3. It is also more in keeping with the complete absence of any colour change in the solutions, even in cases where the oxides dissolve rapidly.

It was important for our theory to be sure that dithionate formation never occurred in reductions which must involve a two-electron step. No record of any such case has been found in the literature. We have examined a few such reductions, to confirm the results of earlier workers, and found that sulphate and no dithionate is formed in such cases. Sulphurous acid solutions were oxidised by lead dioxide, mercuric oxide, and mercuric chloride respectively, and in each case only traces of dithionate were obtained which could arise from direct oxidation of the $H_2S_2O_5$. Since the reduction of lead dioxide and mercuric oxide to bivalent lead and metallic mercury respectively must occur in a single stage involving two electrons, the absence of dithionate is explained. Reduction of mercuric chloride to mercurous chlorides is also a two-electron step, since the reaction is $2HgCl_2 \longrightarrow Hg_2Cl_2$, and mercurous chloride is $(Hg{\rightarrow}Hg)Cl_2$; absence of dithionate could be similarly explained, but reduction of chlorides is peculiar, and even when only a one-electron step is involved no dithionate may be formed (see Part 2).

The figures for dithionate formation from the two forms of MnO_2 (Table II) necessitate the assumption that the reduction of β-MnO_2 by sulphurous acid, if occurring in two stages, must pass through what amounts to the β-Mn_2O_3 phase. Only in this way could the experimental values for dithionate be explained. It is evident, for example, that, even if it is assumed that the reduction β-$Mn^{IV}O_2 \longrightarrow Mn^{III}$ gave a 100% yield of dithionate, a combination of this step with, say, the manganite (64% dithionate) or α-Mn_2O_3 (83% dithionate) step could not give an overall yield of 95—97% of dithionate. It seems likely that reduction of α-MnO_2 would pass likewise through what amounts to the α-Mn_2O_3 phase.

This deduction assumes that the manganese in β-Mn_2O_3 is all tervalent—which is probable from Zachariasen's work (*loc. cit.*). If it were really $Mn^{II}Mn^{IV}O_3$ it could not form the second step in a reduction of β-MnO_2 occurring in two one-electron steps. The second step would have to be taken as some unknown form of Mn_2O_3 other than α-Mn_2O_3 or manganite.

2. Oxidation by Ferric and Cupric Salts.

Ferric Salts.—Ferric hydroxide and ferric salts occupy rather an important position in connection with the mechanism by which sulphurous acid on oxidation gives dithionate (Bassett and Henry, *loc. cit.*, p. 919). We have confirmed the results obtained by Gélis and by Carpenter (*loc. cit.*) in the reduction of ferric hydroxide by sulphurous acid and have also examined the oxidation of sulphurous acid by ferric salts with some striking results.

Suitable ferric salts are not numerous. We have used the sulphate, nitrate, and chloride in approx. 0·1 equivalent-normal solution (*e.g.*, $FeCl_3$/30 in g. per l.). A solution ten times this strength was also used in the case of the chloride. All the solutions became deep reddish-brown when sulphur dioxide was passed in but this colour faded rapidly.

The ferric sulphate and ferric nitrate solutions gave nearly theoretical yields of dithionate. The 0·1N-ferric chloride converted 53% of the sulphurous acid oxidised into dithionate, although a solution ten times as concentrated gave hardly any dithionate.

0·1N-Nitric acid was found to oxidise sulphurous acid, and 22·8% of the acid oxidised was converted into dithionate. This oxidation by the nitrate had to be allowed for in the ferric nitrate experiment. Addition of hydrochloric acid to the ferric chloride solution greatly reduced the proportion of dithionate which is formed on reduction by sulphurous acid, whereas the effect of added sulphuric acid on the ferric sulphate reaction is quite small.

The experimental results are summarised below.

The behaviour of the sulphate and nitrate solutions is clearly similar to that of the solution of ferric hydroxide in sulphurous acid.

Anions of high electroaffinity such as SO_4'' and NO_3' do not readily form stable complex ions. Complex ferrisulphite anions can accordingly be formed with ease in the sulphate and nitrate solutions and give high yields of dithionate as they undergo oxidation and reduction. The ferrichloride anion $(FeCl_4)'$ is, however, very stable, so that ferrisulphite anions are not so readily formed in the chloride solution.

The following complex ions would appear to be possible in the sulphurous acid solutions prepared from ferric chloride with or without additional chlorions: $[Fe(SO_3)_2]'$; $[FeCl_2(SO_3)]'$; $[FeCl_4]'$. It seems unlikely that any $[Fe(SO_3)_3]'''$ could be present on acr unt of the very low concentration of SO_3'' ions.

Collisions between two $[Fe(SO_3)_2]'$ or one $[Fe(SO_3)_2]'$ ion and either of the other two might give rise to either dithionate or sulphate according to how the two-electron switches occurred.

Collisions between two $[FeCl_2(SO_3)]'$ ions might also yield either dithionate or sulphate, but collisions between $[FeCl_2(SO_3)]'$ and $[FeCl_4]'$ could give only sulphate. Formation of the latter two ions would be favoured by increase in the concentration of any source of chloride ions, even by increase in the concentration of ferric chloride: $2FeCl_3 + H_2SO_3 = H[FeCl_2(SO_3)] + H[FeCl_4]$. It is not surprising therefore to find that although a dilute solution of ferric chloride gives rise to a high proportion of dithionate, a solution of ten times the concentration yields hardly any.

As reduction of the ferric chloride solution takes place all the chloride ions bound in anionic complexes become available for further $(FeCl_4)'$ formation, since the ferrous ion has much less tendency to form complex anions than has the ferric ion. Complex ferrisulphite ions are formed more readily at the commencement of the reduction than later when the proportion of chloride ions increases. Dithionate formation occurs chiefly in the early stages of reduction for this reason.

The effect of added sulphuric acid on the ferric sulphate reaction is to reduce dithionate formation slightly and to slow down the reduction considerably.

The concentration of SO_3'' ions and therefore of ferrisulphite ions is greatly diminished by the addition of sulphuric acid. The collision rate between ferrisulphite ions and their rate of reaction are proportionately depressed. This slowness of reaction under strongly acid conditions appears to render reaction (*a*) more possible than is normally the case, though (*b*) still predominates:

(*a*) $2[Fe(SO_3)_2]' + H_2O = SO_4'' + 2H^{\cdot} + 2Fe^{\cdot\cdot} + 3SO_3''$
(*b*) $2[Fe(SO_3)_2]' = S_2O_6'' + 2Fe^{\cdot\cdot} + 2SO_3''$

The intense colour of the ferrisulphite ions is in full agreement with the well-known effect on colour of having an easily oxidised and an easily reduced group in the same molecule or ion.

Antony and Manasse (*Gazzetta*, 1899, **29**, i, 514) stated that ferric sulphate at 0° gave an 80% yield of dithionate according to the erroneous equation $Fe_2(SO_4)_3 + 3SO_2 + 2H_2O = 2FeS_2O_6 + 2H_2SO_4$ in which half the dithionate formed was supposed to result from combination of SO_2 with sulphate.

Experimental.

Solutions of ammonium ferric alum, sublimed anhydrous ferric chloride, and ferric nitrate, approx. 0·1 equivalent-normal, were saturated with sulphur dioxide and the containers were then tightly corked. All the experiments were carried out at approx. 25°.

The ferric nitrate solution was prepared from a previously analysed solution of ferric chloride which was precipitated with ammonia. The well-washed precipitate was then dissolved by addition of the theoretical amount of a standard nitric acid solution. All the solutions became dark reddish-brown when the sulphur dioxide was passed in. The initial colour was apparently of the same depth with the three solutions to which no additional sulphuric or hydrochloric acid had been added, but in the case of the ferric chloride solution made approximately 0·5N. to free hydrochloric acid it was somewhat paler. After the solutions had become colourless, the sulphur dioxide was displaced by a rapid current of carbon dioxide, complete displacement being confirmed by addition of a drop of 0·1N-iodine.

Analyses of the solutions were carried out by one of the following methods.

(*a*) A small amount of hydrogen peroxide was added to reoxidise the reduced iron (which it does at once). The ferric iron was doubly precipitated by ammonia, and after being well washed was ignited and weighed as Fe_2O_3. The combined filtrates from the ferric hydroxide were acidified with hydrochloric acid and precipitated at 60° barium chloride with constant stirring. To the filtrate and washings from the barium sulphate were added 15 c.c. of concentrated nitric acid for every 100 c.c. of solution, and the mixture was evaporated to dryness on the hot plate. Sufficient barium chloride must be present to combine with all the sulphate resulting from oxidation of dithionate. During the course of

the evaporation all ammonium ions are destroyed by the combined effect of the nitric and hydrochloric acids (a great advantage). The residue was treated with about 10 c.c. of concentrated hydrochloric acid (to replace nitrate by chloride). After evaporation of excess of acid, water was added and the barium sulphate, resulting from oxidation of dithionate was determined.

(*b*) The reduced solution was precipitated with ammonia without prior re-oxidation of the iron, and the black hydroxide precipitate was filtered off, washed, redissolved in hydrochloric acid, and reprecipitated with ammonia. This precipitate filtered very slowly and, owing to the appreciable solubility of ferrous hydroxide, a small amount of ferric hydroxide eventually separated from the filtrate and was filtered off separately. The black partly oxidised hydroxide redissolved readily in hydrochloric acid, but there was always a small amount of (probably) γ-$Fe_2O_3.H_2O$ which would not redissolve without use of excessive amounts of hydrochloric acid or undue heating. There was no need for complete dissolution, however, as the object of the second precipitation was only to remove small amounts of strongly adsorbed sulphate and possibly dithionate. From this point the procedure was the same as with method (*a*).

Method (*a*) is greatly preferable but it was necessary to show that the treatment with hydrogen peroxide did not lead to any destruction of dithionate (though dithionate is very resistant to oxidation).

In two otherwise identical experiments with the ferric alum analyses were made by each method. The results were identical within the limits of accuracy.

Oxidation by Ferric Sulphate.—(i) Ammonium ferric alum solution with no added acid (0·1070 g. of Fe_2O_3 per 50 c.c. = 0·0814 equivalent-normal) became colourless after 5 hours. Analysis by method (*a*) showed that 98·5% of the sulphurous acid oxidised gave dithionate. (ii) In a similar experiment, analysis by method (*b*) showed that 99·1% of the sulphurous acid oxidised gave dithionate. (iii) Ammonium ferric alum of the same concentration as above but 0·5N. with respect to free sulphuric acid required *ca.* 12 hours to become colourless; analysis by method (*a*) showed that 94·5% of the total sulphurous acid oxidised gave dithionate.

Oxidation by Ferric Nitrate.—Fe_2O_3 (0·1363 g.) and the equivalent amount of nitric acid (but no additional acid) were made up 50 c.c. (= 0·1023 equivalent-normal). The initial dark reddish-brown colour obtained on passage of sulphur dioxide faded rapidly but there was still a slight pale brownish colour after 6½ hours, probably due to a trace of nitric oxide. The sulphur dioxide was then displaced by a rapid current of carbon dioxide and the solution became colourless. Analysis was by method (*b*). 0·0992 G. of $BaSO_4$ was obtained from the sulphate, and 0·4210 g. from the dithionate formed. Deducting the corresponding amounts resulting from the sulphate and dithionate produced in 6½ hours by 50 c.c. of 0·1N-nitric acid, which are 0·0986 g. of $BaSO_4$ from sulphate and 0·0295 g. from dithionate, we get 0·0006 g. of $BaSO_4$ from sulphate and 0·3915 g. from dithionate as the amounts formed by the ferric iron. Now if 0·1363 g. of Fe_2O_3 gave 100% oxidation to dithionate there would result 0·3982 g. of $BaSO_4$. Thus, the ferric iron in ferric nitrate, at any rate in 0·1 equivalent-normal solution, gives a nearly 100% yield of dithionate.

Oxidation by Ferric Chloride [all but (iv) analysed by method (*b*)].—(i) 0·0798 Equivalent-normal ferric chloride with no additional acid became colourless after 2½ hours. Of the total sulphurous acid oxidised 53·4% gave dithionate.

(ii) Ferric chloride of the same concentration but 0·1N. with respect to free hydrochloric acid became colourless after 1½ hours; 25·9% of the sulphurous acid oxidised gave dithionate.

(iii) Ferric chloride of the same concentration but 0·5N. with respect to free hydrochloric acid, became colourless in 0·5 hour. Only 2·5% of the sulphurous acid oxidised had formed dithionate.

(iv) Since the effect of added hydrochloric acid was probably due chiefly to the chloride ions the behaviour of approx. equivalent-normal ferric chloride ($FeCl_3$/3 in g. per l.) without added acid was examined. 0·804 Equivalent-normal ferrichloride with no additional acid was used. The initial very dark colour obtained on passage of sulphur dioxide faded very rapidly. After 6 hours the solution was pale, slightly greenish-blue. The sulphur dioxide was then displaced by a rapid current of carbon dioxide, and the solution lost most of its greenish tinge but remained rather greener than a solution of ferrous ammonium sulphate of corresponding concentration, in accord with the fact that the sulphate and dithionate formed showed that only 95·8% of the ferric salt had been reduced. Complete reduction takes a long time in concentrated solutions. Analysis by method (*a*) showed that only 3·0% of the total sulphur dioxide oxidised had yielded dithionate.

Cupric Salts.—Cupric sulphate and nitrate are not reduced by sulphurous acid, but in solutions containing a large excess of alkali sulphite where cuprisulphite anions probably exist reduction to the cuprous condition does occur and about 70% of the sulphite oxidised is converted into dithionate (Baubigny, *Ann. Chim. Phys.*, 1910, **20**, 12; *Compt. rend.*, 1912, **154**, 701). Cupric chloride is reduced by sulphurous acid, and cuprous chloride is precipitated. We found that the oxidation product is sulphate with a very small proportion of dithionate. In this case also, a larger proportion of dithionate is obtained from a 0·1 equivalent-normal cupric chloride than from one of ten times the strength. The reaction evidently takes a course similar to that followed in the case of ferric chloride.

Experimental.

The experiments were carried out at approx. 25°.

Complete reduction of the cupric salt had not occurred in either case. After displacement of sulphur dioxide the copper was precipitated cold with a small excess of potassium hydroxide. The filtrate and

washings were acidified with hydrochloric acid, the sulphate precipitated at 60°, and the filtrate from the barium sulphate oxidised with nitric acid as in other experiments.

(i) 0·1 *Equivalent-normal Cupric Chloride.*—The pale blue solution took on a slight greenish tinge on saturation with sulphur dioxide. The first slight separation of crystals of cuprous chloride occurred after 20 hours. A considerable amount had separated after another 24 hours but was beginning to become discoloured owing to disproportionation $2CuCl \rightleftharpoons Cu + CuCl_2$. The sulphur dioxide was then displaced, and the solution lost its greenish tinge and became pale blue. The precipitated cuprous chloride was filtered off, and the filtrate analysed. The colour of the precipitate obtained with potassium hydroxide indicated that both cupric and cuprous copper must be present. 1·4% of the total sulphur dioxide oxidised had yielded dithionate, and the sulphate plus dithionate obtained corresponded to reduction of 54·4% of the original cupric chloride.

(ii) 1·0 *Equivalent-normal Cupric Chloride.*—The solution became fairly dark yellowish-green on passage of sulphur dioxide. Separation of cuprous chloride began almost at once and a large amount had separated after 19 hours, the solution being still yellowish-green. The precipitate remained quite white. The sulphur dioxide was then displaced, the cuprous chloride removed by filtration, and the solution analysed as above. 81·4% of the original cupric chloride had been reduced and only 0·21% of the sulphur dioxide oxidised had yielded dithionate.

3. The Influence of Dissolved Salts on the Oxidation of Sulphurous Acid Solution by Free Oxygen.

Oxidation of sulphurous acid solution by free oxygen yields sulphuric and dithionic acids. The latter may amount to several per cent. of the total sulphur dioxide oxidised.

The rate of the oxidation is considerably affected by the salts of certain metals, and the relative amounts of sulphuric and dithionic acids may be changed thereby. For example, manganese sulphate greatly increases the quantity of sulphurous acid oxidised, but the increase is entirely in favour of sulphate formation and the amount of dithionate obtained is negligible.

It is generally assumed, by analogy with the oxidation of sodium sulphite solution, that this reaction has a chain mechanism and that the presence of a salt may help to initiate more chains. The effect of the salt on the dithionate formation has received practically no attention.

In 1847 Jacquelain (*Ann. Chim. Phys.*, 1847, [iii], **21**, 110) stated erroneously that sulphurous acid solution was slowly oxidised by air to dithionic acid which was then oxidised to sulphuric acid. The effect of dissolved salts on the sulphurous acid oxidation was first studied by L. Meyer (*Ber.*, 1887, **20**, 3058) who passed a mixture of sulphur dioxide and oxygen through boiling solutions of the salts and estimated the sulphate formed after a definite time. He did not test for dithionate but observed that the oxidation was accelerated considerably by salts of manganese or copper. He listed a number of salts in order of their influence on the reaction. Sulphates and chlorides of Mn, Cu, Fe, and Co, and the sulphates of Ni, Zn, Cd, Mg, cuprous chloride, copper oxide, and even metallic copper had an effect, but thallium and potassium sulphates and sulphuric acid were without effect.

Bachmann (*Ber.*, 1888, **21**, 175) showed that potassium, sodium, and ammonium sulphites were oxidised at similar rates and more quickly than the corresponding hydrogen sulphites or sulphurous acid. The oxidation of pure sodium sulphite solution is slow, according to Titoff (*Z. physikal. Chem.*, 1930, **45**, 641), but may be accelerated by traces of copper, copper sulphate having a noticeable effect in molar concentrations as low as 10^{-13}. The reaction is also retarded by many substances and Bigelow (*ibid.*, 1898, **26**, 493) and Young (*Amer. Chem. J.*, 1901, **23**, 119) examined these. Organic substances like benzyl alcohol were powerful retarding agents and salts such as potassium cyanide, ammonium chloride, and sodium acetate had some effect. In each case Young found the effect greater in alkaline than in neutral solutions, and it appeared from work by Lumière (*Bull. Soc. chim.*, 1950, **33**, 444) that the reactions were not retarded indefinitely, oxidation setting in after a prolonged induction period.

Catalytic acceleration and retardation are closely associated phenomena, and Moureu and Dufraisse have published since 1923 (in the *Compt. rend.*) a large number of papers on the subject. Thus Dufraisse and Horclois (*ibid.*, 1930, **191**, 1126) found that ammonium ferrous sulphate (1%) accelerated the oxidation of a 10% solution of sodium sulphite in water made slightly acid, while the ferric acetylacetone complex retarded it. Ferric hydroxide retarded the oxidation in feebly alkaline solution. Reactions with cobalt salts showed similar effects (Dufraisse and Nakal, *ibid.*, 1932, **194**, 880).

Autoxidation of neutral sodium sulphite solution was shown by Bäckstrom (*J. Amer. Chem. Soc.*, 1927, **49**, 1460) to be a chain reaction. He found, in the photochemical reaction, that each light quantum absorbed caused a great number of molecules to react and since the thermal and photochemical reactions were similarly affected by inhibitors he concluded that the mechanisms of the two reactions must also be similar. The actual mechanism of this oxidation chain is still

in doubt, but Franck and Haber (*Sitzungsber. Preuss, Akad. Wiss. Berlin*, **1931**, 250) treated it as a particular case of their general theory of homogeneous catalysis in aqueous solutions, in which the essential primary process is the " univalent " oxidation of substrate by the catalyst to an unsaturated radical, R_1, which undergoes a second univalent oxidation to reaction product whereby a second radical, R_2, is formed having the properties of a univalent oxidiser. R_2 effects univalent oxidation of substrate with regeneration of R_1. The catalyst is oxidised back to normal by some process and starts a new chain. In the sodium sulphite oxidation the chain is usually started by a heavy-metal ion accidentally present, thus :

$$\left.\begin{aligned} SO_3'' + Cu^{\cdot\cdot} &= SO_3' + Cu^{\cdot} \\ SO_3' + H^{\cdot} &= HSO_3 \ [\equiv R_1] \\ HSO_3 + O_2 + H_2O + SO_3'' &= 2SO_4'' + 2H^{\cdot} + OH \ [\equiv R_2] \\ SO_3'' + OH + H^{\cdot} &= HSO_3 + OH' \end{aligned}\right\} \ Ia$$

The formation of dithionate in such reactions is attributed to dimerisation of HSO_3 or SO_3'. This unknown acid or its anion was postulated as the chain-starting radical since dithionic acid was detected when these reactions took place in the absence of oxygen. Bassett and Henry (*J.*, 1935, 919) were unable to confirm the formation of dithionate either in the oxidation of dissolved sodium sulphite by free oxygen or in the photochemical decomposition of sodium hydrogen sulphite solution in the absence of free oxygen.

The oxidation of sulphite solution proceeded slowly in strongly acid conditions according to Albu and Goldfinger (*Z. physikal. Chem.*, **1932**, **16**, 338), and Haber and Wansborough-Jones (*ibid.*, **18**, p. 103) attributed this to a reduction in the number of sulphite ions in acid solution, it being assumed that the sulphite ions are the most readily oxidised.

Hoather and Goodeve (*Trans. Faraday Soc.*, **1934**, **30**, 1149) found that the rate of oxidation of sulphurous acid catalysed by manganese or ferrous sulphate was depressed by the addition of sulphuric acid although the acid formed by the reaction did not have a marked effect, and Bassett and Henry (*loc. cit.*) showed that the relative amounts of dithionate and sulphate depended on both the acidity and the sulphur dioxide concentration.

Bigelow (*loc. cit.*) recorded that the rate of oxidation of a sodium sulphite solution was proportional to the quantity of air passing through the solution; Miyamoto and Kaya (*Bull. Chem. Soc. Japan*, **1930**, **5**, 123) confirmed this for fairly strong solutions, and in a detailed study of the point (*ibid.*, **1931**, **6**, 264) they found that the rate of absorption increased as the concentration of the sulphite solution increased to 0·35N., remained constant between 0·35N. and 0·75N., and then declined. They concluded that in the interval of constant absorption velocity there were enough sulphite molecules in the surface to react with all the oxygen molecules entering that surface.

Experimental.

Five Dreschel bottles of similar size were connected in series. The first contained 75 c.c. of distilled water and the other four 75 c.c. each of different concentrations of the salt solution under investigation. A current of washed sulphur dioxide was passed through the bottles, immersed in a water thermostat at 25°, until all the solutions were saturated with sulphur dioxide at atmospheric pressure.

A sulphur dioxide–oxygen mixture, issuing from a suitably adjusted flowmeter, was then passed through the five bottles, usually for 15—17 hours. The stream of mixed gases was then replaced by one of carbon dioxide until the excess of sulphur dioxide was displaced (complete freedom being checked with iodine before the solutions were analysed).

The influence of the relative partial pressures of oxygen and sulphur dioxide on the rate of oxidation is shown by the following results.

With the flowmeter adjusted as in all the experiments listed in Tables III—VII and delivering 10 c.c. of oxygen and 23 c.c. of sulphur dioxide per minute, the total oxidation in the first bottle of the first series in Table III was equivalent to 0·08 g. of barium sulphate per hour, which corresponded to only 0·7% of the oxygen passing during this time.

The sulphur dioxide and oxygen jets in the flowmeter were then interchanged, so that the rates of flow were reversed. The total oxidation was increased by more than 40% but no significant change in the dithionate : sulphate ratio was observed. It follows that major variations of partial pressures must be avoided if reproducible results are to be obtained, but small accidental variations are not likely to affect seriously either the rate of oxidation or the proportion of dithionate formed. The necessity for good temperature control is shown by Table III (*c*). All the experiments recorded in Tables III—VII were made at 25°.

When the sulphur dioxide–oxygen mixture was passed through five bottles in series which originally contained water only, saturated with sulphur dioxide at atmospheric pressure, the results given in Tables III (*a*) and (*b*) were obtained. The proportion oxidised to dithionate in the several bottles was constant within the limits of error of the determinations but there was a significant drop in the total

amount oxidised as one went from the first to the last bottle. Since a more than four-fold increase in the partial-pressure ratio $O_2 : SO_2$ only increased the rate of oxidation by 40%, it is not likely that a 0·7% decrease in the amount of oxygen passing would cause a fall of more than 2% in the amount oxidised in the second bottle compared with the first, and some other explanation for the marked decrease from bottle to bottle must be sought. The following seems to be the most likely.

Initially all the bottles contain sulphurous acid saturated with sulphur dioxide at approx. atmospheric pressure. When the oxygen–sulphur dioxide mixture is passed through the bottles, sulphur dioxide is gradually displaced from the solutions until the concentration is reduced to that appropriate to a sulphur dioxide partial pressure of only 23/33 of an atmosphere. During this process the sulphur dioxide displaced is passed on from bottle to bottle so that in effect the solution in each successive bottle undergoes oxidation at a considerably lower oxygen partial pressure than can be accounted for by the small amount of oxygen used up by the oxidation occurring in each bottle. Oxidation at this lower oxygen pressure persists for a larger fraction of the whole period with each successive bottle. In spite of this drawback, the method of experimentation still seemed the most convenient and satisfactory for the object we had in view, as the above effect could easily be allowed for.

The time for each experiment varied somewhat in different experiments, and hence also the total amount of oxidation which occurred in the first bottle.

The amount of barium sulphate which would have been obtained from each bottle, had it only contained sulphurous acid without an added salt, was then calculated by simple proportion from the weight obtained from the first bottle in any series and from the various bottles of Table III (*a*) and (*b*). The difference between the figures so calculated and the experimental figures shown in the third column of the various tables gives the increase or decrease in the amount of oxidation due to the dissolved salt. It is these differences which are given, as percentages, in column 4.

In solutions of sulphates stronger than 0·05M. a large proportion of the total sulphate found by analysis is due to the original salt. This disadvantage led to the use of chlorides, since it was expected that the catalytic effect of a salt would be due entirely to the cation. This expectation was not entirely fulfilled, and both sulphate and chloride were investigated in some cases.

Interference of a series by the salt of a preceding series was not detected. The bottle used for the blank determination (*i.e.*, the first bottle) never contained a salt solution and all the bottles were rinsed with hot distilled water before each series. No organic liquid was used. A strong poisoning effect was noted on one occasion when sulphurous acid without any added salt was being oxidised, and it persisted until traced to some new rubber tubing connecting various parts of the flowmeter. It was presumed that an organic accelerator or antioxidant present in the rubber was responsible. The tubing was replaced by some which had been in use previously and glass-to-glass joints made wherever possible. The poisoning effect disappeared immediately.

Analyses of Solutions after Oxidation.—The solution after oxidation was freed from sulphur dioxide and was made up to 200 c.c. Sulphate and dithionate were determined in separate portions essentially as described by Bassett and Henry (*loc. cit.*, p. 923). The portion to be analysed for dithionate was treated in the cold with barium hydroxide solution in slight excess, and the precipitate of barium sulphate and metal hydroxide filtered off after settling overnight. Dithionate determinations carried out in this way are usually slightly high on account of barium nitrate occluded by the sulphate. A series of determinations made on pure $Na_2S_2O_6.2H_2O$ showed that the mean value was 0·5% high and that the probable error was ±3%. This appears as an error of only ± 0·12% when the dithionate itself only amounts to 4% of the total sulphur dioxide oxidised (as in so many of the experiments below). This is in fair agreement with the corresponding error deduced from the variation of dithionate in the results of the series shown in Tables III (*a*) and (*b*).

Experimental Results.—These are shown in the Tables. " Normality " in Tables IV—VII refers to equivalent-normality, *i.e.*, NaCl, $NiCl_2/2$, $FeCl_3/3$, etc., in g./l.

TABLE III.

Sulphurous acid solutions saturated with SO_2 *at 25°.*

Position in series.	Total SO_2 oxidised ($BaSO_4$, g.).	Change (%) of total oxidation in the series.	SO_2 (%) oxidised to S_2O_6''.	Position in series.	Total SO_2 oxidised ($BaSO_4$, g.).	Change (%) of total oxidation in the series.	SO_2 (%) oxidised to S_2O_6''.
(*a*) *First series.*				(*b*) *Second series.*			
1st	1·2485	—	4·07	1st	1·2304	—	3·83
2nd	1·2208	−2·2	3·88	2nd	1·2024	−2·3	3·84
3rd	1·1623	−6·9	3·95	3rd	1·1400	−7·4	3·90
4th	1·0951	−12·3	4·24	4th	1·0496	−14·7	4·07
				5th	1·0064	−18·2	4·21

Probable error in the determination of the percentage dithionate formed, calc. from the variation from the mean value: (*a*) ±0·16, (*b*) ±0·15%.

(*c*) *Sulphurous acid solutions saturated with* SO_2 *and oxidised at various temperatures.*

Temp.	0	15	25	35—40
SO_2 (%) oxidised to S_2O_6''	4·8	4·6	3·7	2·5

TABLE IV.

Solutions containing hydrochloric acid.

Position in series.	Normality of HCl.	Total SO_3 oxidised ($BaSO_4$, g.).	Change (%) of total oxidation.*	$BaSO_4$ (g.) from S_3O_6''.	SO_3 (%) oxidised to S_3O_6''.
1st	0	2·3607	—	0·0938	4·0
2nd	0·01	2·2730	− 1·5	0·0895	3·9
3rd	0·10	1·9882	− 9·4	0·0777	3·9
4th	0·50	0·9952	−51·3	0·0268	2·7
5th	1·00	0·2904	−85·0	0·0069	2·4

* Values given in this column and in the corresponding columns of Table V are corrected for the positions of the bottles in the series as explained on p.1552.

TABLE V.

Solutions containing sodium chloride.

Position in series.	Normality of salt solution.	Total SO_3 oxidised ($BaSO_4$, g.).	Change (%) in total oxidation.	$BaSO_4$ (g.) from S_3O_6''.	SO_3 (%) oxidised to S_3O_6''.
(*a*) *First series.*					
1st	0	1·7624	—	0·0729	4·1
3rd	0·02	1·8892	15·5	0·0797	4·2
4th	0·07	1·6999	10·4	0·0779	4·6
2nd	0·50	1·4635	−15·0	0·0840	5·8
(*b*) *Second series.*					
1st	0	1·5110	—	0·0675	4·5
2nd	0·50	1·1681	−20·9	0·0676	5·8
3rd	1·00	0·8290	−40·9	0·0510	6·2
4th	2·00	0·5905	−54·8	0·0425	7·2
5th	0	1·2142	−1·8	0·0527	4·3
Solutions containing ammonium salts.					
(*a*) *Ammonium chloride.*					
1st	0	1·8810	—	0·0820	4·4
2nd	0·1	1·8455	0·4	0·0875	4·7
4th	0·5	1·3098	−19·4	0·0778	5·9
3rd	1·0	1·2810	−26·7	0·0810	6·3
5th	2·0	0·9190	−40·3	0·0595	6·5
(*b*) *Ammonium molybdate.*					
1st	0	1·3216	—	0·0600	4·5
2nd	0·001	1·4020	8·5	0·0648	4·6
3rd	0·01	1·0615	−13·4	0·0475	4·5
4th	0·10	0·8131	−28·8	0·0411	5·1
5th	1·0	0·7171	−33·7	0·0541	7·5
Solutions containing magnesium sulphate.					
1st	0	1·6039	—	0·0709	4·4
2nd	0·03	1·9301	23·1	0·0879	4·6
4th	0·08	1·4355	3·5	0·0655	4·6
3rd	0·23	1·3800	−7·3	0·0675	4·9
5th	0·43	1·0810	−17·6	0·0544	5·0
Solutions containing zinc sulphate.					
1st	0	1·5324	—	0·0614	4·0
2nd	0·011	1·6508	9·6	0·0685	4·2
4th	0·033	1·5163	14·3	0·0658	4·3
3rd	0·074	1·4199	−2·1	0·0621	4·4
5th	0·156	1·1981	−4·5	0·0566	4·7
Solutions containing aluminium sulphate.					
1st	0	1·5132	—	0·0669	4·4
2nd	0·022	1·7765	20·2	0·0695	3·9
3rd	0·084	1·4381	2·3	0·0664	4·6
4th	0·23	1·3278	1·5	0·0431	3·2
5th	0·50	0·9020	−27·1	0·0388	4·3

TABLE V.—*continued.*

Position in series.	Normality of salt solution.	Total SO_2 oxidised ($BaSO_4$, g.).	Change (%) in total oxidation.	$BaSO_4$ (g.) from S_2O_4''.	SO_2 (%) oxidised to S_2O_4''.
(*a*) *Solutions containing manganese sulphate.*					
1st	0	0·2474	—	0·0170	6·9 *
2nd	0·011	0·6827	182	0·0115	1·7
3rd	0·103	1·5779	587	0·0019	0·1
4th	0·353	1·7874	735	0·0026	0·1
(*b*) *Solutions containing manganese chloride.*					
1st	0	1·6175	—	0·0697	4·3
2nd	0·01	2·4055	52·2	0·0100	0·4
4th	0·05	4·2304	202	0·0057	0·1
5th	0·10	5·2779	299	0·0054	0·1
3rd	0·20	6·5262	325	0·0050	0·1
(*c*) *Solutions containing manganese chloride (more concentrated).*					
1st	0	1·1022	—	0·0452	4·1
3rd	0·5	4·8938	378	0·0038	0·1
2nd	1·0	4·8355	349	0·0045	0·1
5th	2·8	0·5759	−36·2	0·0041	0·7
4th	4·0	0·3029	−68·2	0·0067	2·2
(*a*) *Solutions containing cobalt sulphate.*					
1st	0	1·1778	—	0·0461	3·9
2nd	0·007	1·5315	33·1	0·0430	2·8
4th	0·03	1·4396	41·2	0·0396	2·8
3rd	0·10	1·5393	40·7	0·0328	2·1
(*b*) *Solutions containing cobalt chloride.*					
1st	0	1·1538	—	0·0510	4·4
2nd	0·007	1·3642	20·9	0·0520	3·8
3rd	0·032	1·1518	7·5	0·0463	4·0
5th	0·054	1·0182	7·8	0·0414	4·1
4th	0·097	1·1103	11·2	0·0438	3·9
(*a*) *Solutions containing nickel sulphate.*					
1st	0	1·4531	—	0·0628	4·3
2nd	0·006	1·8908	33·2	0·0408 *	2·2 *
5th	0·021	1·5173	28·3	0·0373	2·5
3rd	0·070	1·7796	31·9	0·0316	1·8
4th	0·107	1·5851	26·1	0·0381	2·4
(*b*) *Solutions containing nickel chloride.*					
1st	0	1·1661	—	0·0525	4·5
2nd	0·007	1·1817	3·7	0·0501	4·2
3rd	0·027	1·2183	12·5	0·0492	4·0
4th	0·061	1·0962	8·6	0·0426	3·9
5th	0·10	0·8889	−6·8	0·0348	3·9
(*a*) *Solutions containing ammonium ferrous sulphate.*					
1st	0	1·5953	—	0·0690	4·3
2nd	0·006	1·8248	17·1	0·0263	1·4
3rd	0·028	1·6274	9·9	0·0288	1·8
4th	0·08	1·5068	9·2	0·0286	1·9
5th	0·14	1·1940	−8·5	0·0533	4·5
(*b*) *Solutions containing ferrous sulphate.*					
1st	0	1·6806	—	0·0694	4·1
2nd	0·001	1·7138	4·3	0·0480	2·8
3rd	0·01	1·8531	18·7	0·0299	1·6
4th	0·10	1·7688	21·6	0·0633	3·6
5th	1·00	1·0174	−26·0	0·0910	8·9

* Note: the gas flowmeter was not used in this series. The high proportion of dithionate is probably due to the fact that the experiment was stopped at an early stage so that oxidation had occurred in more concentrated solutions than usual.

* Low result due to loss during evaporation with nitric acid.

TABLE VI.

Position in series.	Normality of salt solution.	Total SO_2 oxidised ($BaSO_4$, g.).	Change (%) in total oxidation.	$BaSO_4$ (g.) equiv. to oxidation of SO_2 by single reduction of $Fe^{3+} \longrightarrow Fe^{2+}$.	$BaSO_4$ (g.) from S_2O_6''.	SO_2 (%) oxidised to S_2O_6''.
(*a*) *Solutions containing ferric sulphate.*						
1st	0	1·468	—	0·000 } Double these	0·0535	3·6
2nd	0·015	1·580	10·1	0·044 } amounts for	0·0571	3·6
3rd	0·15	1·885	38·3	0·437 } dithionate	0·5718	30·3
4th	1·50	5·554	337	4·376 } formation	4·6210	83·2
(*b*) *Solutions containing ferric chloride.*						
1st	0	1·580	—	0·000	0·0560	3·5
2nd	0·02	2·538	64·4	0·058	0·0533	2·1
3rd	0·21	3·004	106	0·613	0·0443	1·5
4th	2·86	8·024	487	8·344	0·0179	0·2

TABLE VII.

Position in series.	Normality of salt solution.	Total SO_2 oxidised ($BaSO_4$, g.)	Change (%) in total oxidation.	$BaSO_4$ (g.) from S_2O_6''.	SO_2 (%) oxidised to S_2O_6''.
(*a*) *Solutions containing cupric sulphate.*					
1st	0	1·1931	—	0·0642	5·4
3rd	0·011	0·7216	−34·9	0·0244	3·4
2nd	0·028	0·8549	−26·7	0·0261	3·1
5th	0·087	1·1539	18·2	0·0191	1·7
4th	0·190	1·7132	66·0	0·0144	0·8
(*b*) *Solutions containing cupric chloride. 1st series.*					
1st	0	2·0012	—	0·0612	3·1
4th	N/20,000	1·4644	−15·4	0·0676	4·6
3rd	N/2,000	1·2158	−34·6	0·0710	5·8
2nd	N/200	0·5402	−72·4	0·0402	7·4

Position in series.	Normality of salt solution.	Total SO_2 oxidised ($BaSO_4$, g.).	Change (%) in total oxidation.	$BaSO_4$ (g.) equiv. to oxidation of SO_2 by single reduction of $Cu^{2+} \longrightarrow Cu^{+}$.	$BaSO_4$ (g.) from S_2O_6''.	SO_2 (%) oxidised to S_2O_6''.
(*c*) *Solutions containing cupric chloride. 2nd series.*						
1st	0	1·7493	—	0·0	0·0742	4·2
2nd	0·011	0·5659	−67·0	0·048	0·0256	4·5
3rd	0·032	0·9263	−43·4	0·140	0·0221	2·4
4th	0·069	1·5538	1·0	0·302	0·0196	1·3
5th	0·188	2·0151	36·0	0·822	0·0261	1·3
(*d*) *Solutions containing cupric chloride. 3rd series.*						
1st	0	2·4368	—	0·0	0·1037	4·3
2nd	0·1	1·9619	−17·6	0·438	0·0339	1·7
3rd	1·0	7·6805	244	4·376	0·0293	0·4
4th	2·0	12·5335	495	8·752	0·0283	0·2

DISCUSSION.

Tables III—VII show that the electrolytes examined can be divided into several groups according to the influence they exert on the oxidation of sulphurous acid by molecular oxygen.

(i) Hydrochloric acid retards the oxidation and lowers the dithionate : sulphate ratio.

(ii) Salts of Na, NH_4, Mg, Zn, and Al seem to accelerate the oxidation a little at low salt concentrations, but they definitely retard the reaction when the concentration is much above 0·05N. The proportion of dithionate either is unaffected or increases somewhat at higher salt concentrations, more particularly with sodium and ammonium salts.

(iii) The total oxidation is enormously increased in presence of manganese salts. An increase is found with salt concentrations as low as N/10,000 (as shown by a few exploratory tests not recorded in the Tables) and rapidly becomes greater as the salt concentration increases. It eventually falls off at salt concentrations above about 2N.; manganese sulphate is a much more potent catalyst than the chloride. The increased oxidation is entirely caused by sulphate

formation. Dithionate is, to a great extent, suppressed, the absolute amount which is formed being reduced to about a tenth of that obtained in absence of the manganese salt.

(iv) Cobalt and nickel sulphates appear to act similarly to manganese salts; they cause a considerable though much smaller increase in the rate of sulphate formation. Unlike manganese salts they do not greatly reduce the absolute amount of dithionate formed. The increased oxidation brought about by cobalt and nickel chlorides is much smaller, being of the same order as that caused by Na, NH_4, Mg, Zn, and Al salts.

(v) Ferrous sulphate appears to have a small catalytic activity. There is some evidence that a part of this is caused by oxidation to the ferric salt by molecular oxygen, followed by reduction of the ferric salt.

(vi) Ferric and cupric salts appear to act both catalytically and as direct oxidants. Very low concentrations of copper salts cause a marked *retardation* of the oxidation.

The chain reaction mechanism put forward by Franck and Haber (*loc. cit.*) for the oxidation of sodium sulphite by gaseous oxygen, in which the chains are initiated by small quantities of heavy-metal ions such as copper, may well play an important part in the reaction but appears to be inadequate by itself to explain all the observations on the oxidation of concentrated sulphurous acid solutions in presence of different salts. Very low concentrations of copper salts (*e.g.*, M/40,000) are found to *retard* the oxidation and, although manganese salts in small concentration do accelerate the oxidation, the chain mechanism does not explain how the formation of dithionate is suppressed. If dithionate resulted from dimersation of the hypothetical HSO_3, as in Franck and Haber's chain mechanism, its amount should increase with an increase in the number of chains, while the amount of dithionate resulting from an independent mechanism (*e.g.*, oxidation of $H_2S_2O_6$) should remain independent of the manganese concentration.

The fact that the uncatalysed atmospheric oxidation of alkali sulphite solutions is more rapid than that of sulphurous acid solutions of equivalent concentrations (Bachmann, *loc. cit.*), taken in conjunction with the effect of acid on the oxidation of sulphurous acid (Table II), makes it probable that it is ions which are oxidised rather than un-ionised molecules. These ions may be SO_3'', HSO_3', S_2O_6'', or HS_2O_6'. They may be supposed to have some tendency to add an oxygen molecule by co-ordination to a sulphur atom. These complexes could take part in the Franck–Haber chain mechanism even better than the separate ions and oxygen molecules. Sulphate could result from $(O_2{\rightarrow}SO_3)''$ or $(O_2{\rightarrow}SO_3H)'$, and dithionate from $(O_4{\rightarrow}S_2O_6)''$ or $(O_2{\rightarrow}S_2O_6H)'$. The equations for two such reactions could be:

$$\left.\begin{array}{rl} & HSO_3 + (O_2{\rightarrow}SO_3)'' + H_2O = 2SO_4'' + 2H^{\cdot} + OH \\ & SO_3'' + OH + H^{\cdot} = HSO_3 + OH' \end{array}\right\}$$

and

$$\left.\begin{array}{rl} & HSO_3 + (O_2{\rightarrow}HS_2O_6)' + H_2O = HSO_4' + HS_2O_6' + H^{\cdot} + OH \\ & SO_3'' + OH + H^{\cdot} = HSO_3 + OH' \end{array}\right\}$$

} Ib

Added acid, in so far as it shifted the reactions

$$H^{\cdot} + SO_3'' \longrightarrow HSO_3' \xrightarrow{+H^{\cdot}} H_2SO_3 \xrightarrow{+SO_2} H_2S_2O_6 \longrightarrow H_2O + 2SO_2$$

$$HSO_3' + SO_2 \longrightarrow HS_2O_6'$$

from left to right would tend to increase the proportion of dithionate to sulphate formed on oxidation, but since the SO_3'' would almost disappear after the addition of very little acid and since the reaction $HSO_3' + SO_2 \rightleftharpoons HS_2O_6'$ is virtually independent of the acidity this effect would not be easily detected with sulphurous acid solutions. Total sulphur dioxide solubility will decrease at higher acidities, and the rate of formation of both sulphate and dithionate will tend to decrease in consequence but not necessarily at the same rate. The experimental results show that dithionate formation falls off more quickly than that of sulphate.

In addition to reactions of the Franck–Haber type it would appear possible for reactions such as the following to occur independently, though more slowly.

$$\left.\begin{array}{ll} (a) & (O_2{\rightarrow}SO_3H)' + HSO_3' = 2HSO_4' \\ (b) & (O_2{\rightarrow}S_2O_6H)' + HS_2O_6' = 2HS_2O_6' \end{array}\right\} \text{II}$$

The relatively small increase in the rate of oxidation which is brought about by the presence of salts of Na, NH_4, Mg, Zn, and Al in low concentration can probably be accounted for satisfactorily by the normal "neutral salt effect." This should cause an *increase* in the rate of

reaction between *similarly charged ions* such as those involved in reactions II but would not be expected to affect reactions of the Franck–Haber type.

Dithionate formation is little affected by low concentrations of these salts. The diminished rate of oxdiation with higher concentrations of the same salts is presumably due chiefly to decreased solubility of oxygen.

Manganous salts have a far greater catalytic effect on the sulphurous acid oxidation than have any other salts examined. The rate of sulphate formation is enormously increased, while dithionate formation is almost completely suppressed.

It is suggested that the catalytic effect of $Mn^{\cdot\cdot}$ can be explained by supposing that a $[Mn(SO_3)_2]''$ or similar ion adds an oxygen molecule very readily both by direct addition and by depriving $(O_2{\rightarrow}SO_3)''$ and similar complexes of their O_2, thus:

$$(O_2{\rightarrow}SO_3)'' + [Mn(SO_3)_2]'' = (SO_3)'' + [O_2{\rightarrow}Mn(SO_3)_2]''$$

The new complex undergoes rapid rearrangement

$$[O_2{\rightarrow}Mn(SO_3)_2]'' = [Mn(SO_4)_2]'' \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad \text{III}$$

but since ions of low electro-affinity such as $(SO_3)''$ will tend to replace those of high electro-affinity any complex sulphate ion such as the above would break up and fresh sulphite complexes would be formed. The effect of the manganese is thus to replace the chain reactions I*a* and I*b*, and reactions such as those shown in equation II(*a*) and II(*b*) by an entirely different mechanism III. This will yield practically nothing but sulphate, because complexes containing $(S_2O_3)''$ ions will have little tendency to be formed, both on account of the high electro-affinity of $(S_2O_3)''$ in comparison with $(SO_3)''$ and for steric reasons.

The catalytic effect of cobalt, nickel, and ferrous sulphates is much less than that of manganese sulphate, but more marked than that of magnesium or zinc sulphates. Dithionate formation is reduced but not almost suppressed as with manganese. The results observed are consistent with the view that the increased oxidation brought about by these three salts is partly caused by the " neutral salt effect " and partly by a true catalysis involving complex anions containing added oxygen of a type similar to the manganese complex. The total oxidation in the presence of cobaltous, nickel, or ferrous salts would thus involve three quite different mechanisms, of the types illustrated by equations I*a*, I*b*, II, and III.

The presence of chloride ions interferes with the formation of the sulphite complexes because of the stability of complex chloride ions (see Part 2). It is for this reason that the catalytic activity of cobalt and nickel chlorides is practically nil, while that of even manganese chloride is only from one-third to one-half of that of the sulphate at similar concentrations.

Manganese chloride is as active in suppressing dithionate formation as is manganese sulphate. This suggests that $(MnCl_4)''$ ions are just as able to deprive $[O_2{\rightarrow}SO_3]''$ complexes of their oxygen molecule to form $[O_2{\rightarrow}MnCl_4]''$ as are the $[Mn(SO_3)_2]''$ ions to form $[O_2{\rightarrow}Mn(SO_3)_2]''$. The result is that, while the whole of the manganese present is effective in suppressing the original mechanisms of types I*a* and I*b* with their dithionate formation, only from one-third to one-half carries on the oxidation by the new mechanism. There will be some equilibrium between $[O_2{\rightarrow}MnCl_4]''$ and $[O_2{\rightarrow}Mn(SO_3)_2]''$ complexes, and the catalytic effects suggest that the concentration of the chloride complexes is about twice that of the sulphite complexes. The metal sulphates are so much less soluble than the chlorides that only sulphate solutions of comparatively low concentrations can be examined for catalytic activity. When the salt concentrations are high enough—even with manganese salts—oxidation of sulphurous acid falls off greatly owing to decreased solubility of oxygen or sulphur dioxide or both.

If the strength of the $O_2{\rightarrow}$metal link is too great, then, while the complex oxygen–(metal sulphite) ions will be formed, their stability may be such that further reaction may be slow. This appears to be the situation with ferrous sulphate (Table V). The results suggest that the salt increases the rate of reaction more than would be expected from the mere neutral salt effect, while the decrease in dithionate formation at low salt concentrations suggests a marked change in the reaction mechanism although at higher salt concentrations there are indications of a large *increase* in dithionate formation. Now the ferrous ion has itself a marked tendency to be oxidised, so that it is probable that O_2 would form the $[O_2{\rightarrow}Fe(SO_3)_2]''$ complex even more readily than that containing manganese. This would prevent the original I*a* and I*b* mechanisms. Owing to the reluctance of the iron atom to part with the oxygen the subsequent reaction is little faster than the oxidation which occurred in absence of the iron but its mechanism is quite different. It appears as if two quite different reactions occurred, *viz.*:

(i) some of the $[O_2 \rightarrow Fe(SO_3)_2]''$ reacts as does the corresponding manganese complex to give $[Fe(SO_4)_2]''$ which then breaks up to give SO_4'';

(ii) some of the complex reacts in such a way that the iron is oxidised to the ferric state. The reaction might be :

$$2[O_2 \rightarrow Fe(SO_3)_2]'' + 2H^{\cdot} = 2Fe''' + H_2O + 3(SO_4)'' + (SO_3)''$$

The ferric iron would be converted into a sulphite complex such as $[Fe(SO_3)_2]'$, some of which would slowly undergo self-oxidation and -reduction with formation of dithionate but practically no sulphate (see Part 2). At low concentrations of ferrous salts the reaction chiefly follows course (i), which is largely independent of concentration, but higher concentrations help the higher-order reaction (ii) so that there is an increase in the proportion of dithionate.

It follows that if these deductions are sound we have a substantiated example, in the case of the ferrous reaction, of a catalysed oxidation which really is caused, in part at least, by a true alternating oxidation and reduction of the catalyst. It is also plain that such a mechanism is exceptional in the case of oxidations catalysed by metal salts and that, as a rule, the catalyst hands on the oxygen by a process which does not involve a true oxidation of the catalyst.

There are some unusual features about the results obtained with ferric sulphate and chloride (Table VI). In particular, the amount of oxidation occurring in the less concentrated chloride solutions is considerably greater than in comparable sulphate solutions. This is the opposite to what is found in other cases. The small increase in total oxidation in the most dilute sulphate solution appears to be a pure neutral salt effect since the proportion of dithionate formed is unaffected.

With higher concentrations of ferric sulphate, its reduction occurs with the high yield of dithionate characteristic of this reaction. A small catalytic effect due to the ferrous salt produced is probably superimposed on the primary reaction. There are no indications that the ferric ion has any direct catalytic action.

The greatly increased oxidation of sulphurous acid in the ferric chloride solutions suggests that the ferric salt is the oxidising agent in this case. It may well be that the $O_2 \rightarrow$metal link is so weak in the case of ferric iron that an oxygen addition complex either is not formed at all with ferric salts or is very unstable. As soon as the ferric ion has been reduced by such reactions as have been discussed in Part 2 of this paper, then the ferrous ion formed would add oxygen with the consequences already discussed in connection with the oxidation catalysed by ferrous sulphate (Table V). This suggests that the oxidation shown in Table VI (*b*) is probably caused by alternate reduction and oxidation of ferric and ferrous complexes.

Cupric sulphate and chloride differ from all other salts we have examined in showing a marked poisoning action on the sulphurous acid oxidation at concentrations below about 0·025M. Above this concentration they show a positive catalytic action which can be quite marked even in 0·1M-solutions [Table VII (*a*, *b*, *c*, *d*)]. Both sulphate and dithionate formation are reduced by the poisoning action which is presumably caused by breaking of the normal oxidation chain.

This inhibiting action of very low copper concentrations is of particular interest because the cupric ion was selected by Franck and Haber (*loc. cit.*) as a possible agent for initiating the chain mechanism suggested by them. It may be that cupric ions could function in this way in much more dilute sulphurous acid solution than those examined by us, but it certainly appears as if any chain mechanism operating in these concentrated solutions must be started in some other way.

In concentrated sulphurous acid solutions the reactions with copper ions in presence of oxygen may be as follows : *

(A) $Cu^{\cdot\cdot} + 2SO_3'' \rightleftharpoons [Cu(SO_3)_2]''$

(B) $\begin{cases} 2[Cu(SO_3)_2]'' + H_2O = 2Cu^{\cdot} + SO_4'' + 3SO_3'' + 2H^{\cdot} \\ 2[Cu(SO_3)_2]'' = 2Cu^{\cdot} + S_2O_6'' + 2SO_3'' \end{cases}$

(C) $Cu^{\cdot} + 2SO_3'' \rightleftharpoons [Cu(SO_3)_2]'''$ $[Cu(SO_3)_2]''' + O_2 \rightleftharpoons [O_2 \rightarrow Cu(SO_3)_2]'''$

(D) $[O_2 \rightarrow Cu(SO_3)_2]''' + HSO_3^{\cdot} = Cu^{\cdot\cdot} + 2SO_4'' + HSO_3'$

(E) $[O_2 \rightarrow Cu(SO_3)_2]''' = Cu^{\cdot} + 2SO_4''$

(F) $2[O_2 \rightarrow Cu(SO_3)_2]''' + 2H^{\cdot} = 2Cu^{\cdot\cdot} + 3SO_4'' + SO_3'' + H_2O$

* Although the concentration of SO_3'' would be low relatively to that of SO_3H', the SO_3'' seems more likely to be the constituent of the complex ions. Similar reactions could occur with complexes built up with SO_3H' ions but would be rather more complicated.

(A) Cupric ions are converted into complex sulphite anions.

(B) These complex anions undergo self-oxidation and -reduction, giving both sulphate and dithionate (Baubigny, *loc. cit.*).

(C) The cuprous ions formed in (B) are converted into oxygen–sulphite complex anions.

(D) This gives a possible way in which the normal oxidation chains are broken. In these chains the neutral HSO_3 is supposed to be the chief active agent.

(E) Most of the oxidation of sulphurous acid now proceeds by this mechanism.

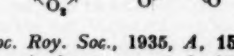
(F) Dithionate formation is never reduced to such a low value in the oxidation catalysed by copper salts as in that catalysed by manganese. This suggests that some cuprous copper is continually being reoxidised by reactions such as (F) and some dithionate being formed by reaction (B).

The above scheme seems to explain all the observed peculiarities of the oxidation catalysed by copper salts, and although it may appear to be complicated it is really made up of a number of quite simple reactions.

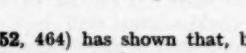
There is justification for the assumption of addition complexes containing molecular oxygen attached to metal atoms or ions. Several examples of complexes of this type can be cited: (1) the oxy-cobalt salts, *e.g.*, $[Co_2(NH_3)_{10}O_2](NO_3)_4$ and the anhydroxy-cobalt salts, *e.g.*, $[Co_2(NH_3)_{10}O_2](NO_3)_5$ (Fremy, *Annalen*, 1852, **83**, 227, 289; Werner, *Z. anorg. Chem.*, 1898, **16**, 245) furnish perhaps the most striking examples of complex salts containing co-ordinated molecular oxygen. Werner supposed that these compounds were true peroxides in which the oxygen was linked to each cobalt atom by a normal co-valency. This involved the assumption that in the anhydroxy-salts half of the cobalt had a valency of four and the other half of three; in the oxy-cobalt salts all the cobalt was tervalent. The reactions of these compounds are not in accordance with these assumptions, whereas they agree with the view that the oxy-cobalt compounds contain only bivalent cobalt while the anhydroxy-cobalt salts contain one atom of bi- and one of ter-valent cobalt. Thus Gluud, Keller, and Nordt (*Ber. Ges. Kohlentech.*, 1933, **4**, 210) showed that, under suitable conditions, solutions of the oxy-cobalt salts break up on heating with almost quantitative regeneration of oxygen and *cobaltous* salt. Werner showed that after treatment of the anhydroxy-salts with concentrated hydrochloric acid 48% of the cobalt could be isolated as $[Co(NH_3)_5Cl]Cl_2$ while the rest could be obtained from the filtrate of the latter as cobaltous sulphate. Only 5% of the cobalt in the oxy-cobalt salts could be isolated as $[Co(NH_3)_5Cl]Cl_2$ but all the rest was obtainable as cobaltous sulphate. Hence the compounds are not true peroxides but must contain co-ordinated oxygen molecules as shown by the formulæ $[(NH_3)_5Co^{II}\leftarrow O_2\rightarrow Co^{II}(NH_3)_5](NO_3)_4$ and $[(NH_3)_5Co^{II}\leftarrow O_2\rightarrow Co^{III}(NH_3)_5](NO_3)_5$.

(2) In oxyhæmoglobin, molecular oxygen is presumably co-ordinated to the iron (ferrous) atom.

(3) According to Traube (*Ber.*, 1916, **49**, 1670) the tetroxides of the alkali and alkaline-earth metals are addition complexes of the peroxides and molecular oxygen, while the "ozonates" of the alkali metals are similar complexes of the alkali-metal hydroxides. The compounds could be formulated as



and



(4) Roberts (*Proc. Roy. Soc.*, 1935, *A*, **152**, 464) has shown that, by suitable treatment in oxygen a tungsten wire becomes coated with oxygen so that oxygen atoms cover about nine-tenths of the surface and oxygen molecules the remaining tenth. The oxygen molecules are driven off quite quickly when the wire is heated in a vacuum to about 80° but the atomic layer remains up to nearly 1700°.

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All the work described in this paper was carried out at the University of Reading, except for a few experiments which were found to be necessary during the final preparation of the paper. These were done in the chemical laboratories of the Tanganyika Geological Survey at Dodoma. The senior author thanks the Director of the Survey, Mr. G. M. Stockley, for the facilities accorded him.

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TANGANYIKA GEOLOGICAL SURVEY, DODOMA.

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353. *The Growth of an Aneurin-requiring Yeast Strain in Various Substrates related to the Tricarboxylic Acid Cycle.*

By S. Jackson and B. C. Kilkenny.

A pure strain isolated from brewery yeast proved to be unusual in being independent of growth factors other than aneurin.

In a glucose–ammonium sulphate medium, the total cell population was proportional to the aneurin concentration up to 10^{-8} M., whereas down to 10^{-9} M., and in much higher aneurin concentrations, the growth rate was constant. The aneurin is thus either a necessary structural unit or, if a catalyst, one which is consumable.

With ammonium sulphate as the nitrogen source, acetate was the only carbon source which supported growth in the absence of aneurin. Even in its presence, certain substances which are intermediates in the tricarboxylic acid cycle (Krebs) did not support growth.

With glucose as the carbon source, amino-acids supported growth only in the presence of aneurin. The growth rate was not increased by serial sub-culture in these media. The highest rate was attained with ammonium sulphate or asparagine as the nitrogen source; with other amino-acids the rate was lower, probably because it was limited by the rate of de-amination.

Origin of the Strain.—A brewery yeast was grown at 25° in an aerated synthetic medium containing glucose, ammonium sulphate, certain growth factors, and small amounts of inorganic salts, buffered to pH 5 with sodium dihydrogen phosphate. Growth was vigorous under these conditions and after six sub-cultures in the synthetic medium, the yeast was plated out on wort agar and individual colonies were selected.

The single colony strains were serially sub-cultured in the synthetic medium incorporating six growth factors. From these series, test transfers were made to similar media, each lacking one of the original six growth factors. The strains were found to be of two types. One was able to grow well in all media containing biotin, but only very slowly, at least initially, in its absence. The other was able to grow vigorously in all the media which contained aneurin, but in its absence only to slight extent in the first sub-culture and not at all in the second. Such a strain is unusual; there appears to be no report in the literature of a strain solely dependent on aneurin (cf. Atkin, *Wallerstein Lab. Comm.*, 1949, xii, **37**, 141).

A single cell was isolated from one of the aneurin-dependent strains, and the experiments to be described were all carried out with cultures originating from this.

Growth of the Strain in Glucose–Ammonium Sulphate Medium containing an Ample Supply of Aneurin.—A detailed examination was made of the growth characteristics of the strain in media containing glucose as the carbon source and ammonium sulphate as the nitrogen source.

The media (Dr. Barton Wright) were made by mixing solutions as follows, under sterile conditions: 10 ml. of glucose solution (50 g./l.); 10 ml. of NaH_2PO_4 solution (3·9 g./l.; pH 5); 5 ml. of a solution containing $(NH_4)_2SO_4$ (10 g./l.), $MgSO_4.7H_2O$ (2·5 g./l.), $CaCl_2$ (1·3 g./l.), KI (0·5 mg./l.), boric acid (0·5 mg./l.), $MnSO_4.4H_2O$ (0·2 mg./l.), $ZnSO_4$ (0·1 mg./l.), $CaSO_4$ (0·1 mg./l.), ammonium molybdate (0·1 mg./l.), and $FeSO_4.7H_2O$ (0·1 mg./l.).

To this medium, growth factor solutions were added as required. Thus, to complete the standard aneurin medium, 0·1 ml. of a solution containing 0·5 mg. of aneurin hydrochloride per l. was added; to complete the fully enriched medium, the other growth factors were added as follows: 0·1 ml. each of calcium D-pantothenate solution (0·5 mg./l.), nicotinic acid solution (0·5 mg./l.), pyridoxine hydrochloride solution (0·5 mg./l.), inositol solution (2·5 mg./l.), and biotin solution (0·5 mg./l.).

The cultures were kept at 25° ± 0·05° in a water-bath and were aerated with filtered air.

In all glucose media there was only a very short lag, followed by a phase of rapid, logarithmic growth which ended when the yeast population reached 50—200 million cells/ml.; thereafter, growth became slow and was not very reproducible in rate or extent. The rate of logarithmic growth, however, was satisfactorily reproducible.

Growth rates were obtained by determining the yeast populations of samples taken at suitable intervals. A Spekker absorptiometer was used to measure the light transmission; it was calibrated against counts of cell population made with microscope and hæmocytometer. The mean generation time, *i.e.*, the time taken for the cell population to double, is the most convenient expression of growth rates.

The mean generation time in the standard aneurin medium was 120 minutes and the final population was about 500 million cells/ml. These remained unchanged when the other growth factors were added and when the aneurin concentration was increased by factors of 10, 100, 1000, or 10,000. The behaviour was the same whether the growth factors were sterilized by heat or by filtration through a bacterial filter. It is clear that the growth factor requirements of the strain are entirely satisfied by the standard aneurin concentration.

In a medium made up without growth factors, growth was limited by exhaustion of the small amount of aneurin carried over with the inoculum from the parent culture. Growth only occurred to this slight extent with uracil in place of aneurin.

Growth of the Strain in Glucose–Ammonium Sulphate Medium containing only Small Amounts of Aneurin.—In Fig. 1, the final populations attained in media containing low aneurin concentrations are plotted against the aneurin concentration. The final population is directly proportional to the aneurin concentration below about 10^{-6} M. The standard concentration was $6{\cdot}7 \times 10^{-7}$

Dependence of final population on:

FIG. 1.

Aneurin concentration.

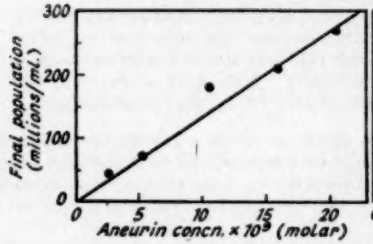


FIG. 2.

Ammonium sulphate concentration.

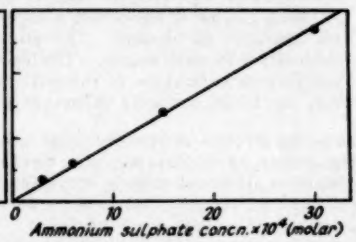
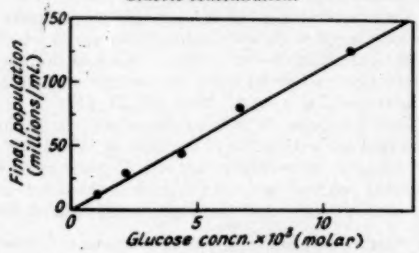


FIG. 3.

Glucose concentration.



M.; in the standard aneurin medium the population must be limited by factors other than the exhaustion of aneurin.

From the slope of the line in Fig. 1, it is possible to calculate the number of aneurin molecules required for the synthesis of each yeast cell. Each cell requires $\frac{22{\cdot}4 \times 10^{-6} \times 6 \times 10^{23}}{300 \times 10^{6}} = 4{\cdot}5 \times 10^{4}$ molecules of aneurin.

It is interesting to compare this figure with the corresponding requirements of glucose and ammonium sulphate. Plots of final population against nutrient concentration over the limiting ranges are shown in Figs. 2 and 3. From the slopes, similar calculations can be made. Each cell requires $\frac{13{\cdot}3 \times 10^{-3} \times 6 \times 10^{23}}{150 \times 10^{6}} = 5 \times 10^{10}$ molecules of glucose and $\frac{32{\cdot}8 \times 10^{-4} \times 6 \times 10^{23}}{300 \times 10^{6}} = 6{\cdot}5 \times 10^{9}$ molecules of ammonium sulphate.

Evidently each molecule of aneurin catalyses the metabolism of about one million molecules of one of the substantial nutrients.

Since the final population is proportional to the aneurin concentration over the appropriate

range, it is evident that aneurin does not function as a simple catalyst. Probably it is incorporated in the structure of the yeast cell or consumed at a constant rate in some other way.

If the aneurin functions as a co-enzyme (cocarboxylase has been identified as aneurin pyrophosphate) it should be diffusible and the growth rate should decrease as the aneurin concentration is lowered.

There is no sign that this occurs. Table I contains the results of an experiment designed to examine the growth rate of the strain in solutions of low aneurin content. To provide a direct comparison, Spekker instrument readings are listed. The method of measurement is not applicable to yeast populations of less than one million cells/ml., so that it was not convenient to make measurements at aneurin concentrations below 10^{-9} M.

TABLE I.

The Growth Rate of the Strain in Solutions of Low Aneurin Content.

Samples were taken from cultures grown in different aneurin concentrations, at the time intervals shown in the first column.

The Spekker absorptiometer readings of the samples are listed under the headings giving the aneurin concentration.

Time intervals (mins.).	Aneurin concentration (moles per l.).					
	$6{\cdot}7 \times 10^{-7}$.	$3{\cdot}3 \times 10^{-7}$.	$1{\cdot}5 \times 10^{-7}$.	$2{\cdot}1 \times 10^{-8}$.	$1{\cdot}1 \times 10^{-8}$.	$2{\cdot}7 \times 10^{-9}$.
0	0·50	0·50	0·50	0·52	0·51	0·52
90	0·46	0·46	0·47	0·46	0·47	0·51
180	0·47	0·41	0·44	0·36	—	0·44
300	0·31	0·33	0·34	0·16	0·37	0·28
390	1·23	1·20	1·22	1·15	1·21	1·22
Final population	390	570	420	270	180	44

The range of population covered in the table is from 2 to 20 million cells per ml. The discontinuous change between the fourth and fifth readings is due to a new standardisation of the Spekker absorptiometer.

Growth of the Strain in Alternative Sources of Carbon or Nitrogen.—The rôle of aneurin in the metabolism of our yeast strain was further investigated by examining the characteristics of growth with different sources of carbon or nitrogen.

Tests were made in media containing the standard aneurin concentration and in aneurin-free media. 10 Ml. of a solution of the new carbon source, at a concentration of 15, 20, or 25 g./l., adjusted to pH 5 with sodium hydroxide, was used in place of 10 ml. of glucose solution. For tests of new sources of nitrogen, ammonium sulphate in the "inorganic solution" was replaced by an amino-acid at a concentration of 6 or 10 g./l. 5 Ml. of this solution were used in making up each tube of medium.

Cultures in which growth was feeble were aerated by shaking. Special tubes, which could be mounted in the Spekker absorptiometer, were used. The light transmission of the whole culture could thus be measured, eliminating the need for sampling.

The results of these experiments are collected in Table II. The most striking features are the unique property of acetate in supporting growth in the absence of aneurin, and the failure of aconitate, citrate, α-ketoglutarate, and oxaloacetate to support growth even in its presence.

The final population in a glucose medium is much greater than that in carboxylic acid media. This is probably because growth is limited by different factors. During the growth of a culture in glucose, the medium becomes more acid, but this does not have a serious effect until the final pH of 2 units is reached; however, in carboxylic acid cultures the medium becomes more alkaline as the acid is consumed, and yeast does not flourish in these conditions.

Amino-acids support a relatively higher final population than ammonium sulphate, probably because the pH scarcely changes at all during growth in amino-acid media.

Although serial sub-culture leads to an increase in the growth rate in most of the carboxylic acid media, this is not the case in amino-acid media. Ammonium sulphate, and asparagine from which ammonia may be readily obtained, supports the highest growth rate; it is not increased when 26 amino-acids are supplied, in contrast to the behaviour of *Bact. lactis aerogenes* (Stephens and Hinshelwood, *J.*, 1949, 2516). According to Thorne (*J. Inst. Brewing*, 1945, **51**, 114), the growth rate of yeast in amino-acid media may be limited by the rate of de-amination. This appears to be the case with our yeast strain.

Metabolism of Carbon by the Yeast Strain.—Acetate is unique among the carbon sources in supporting growth in the absence of aneurin. It might, therefore, be supposed that aneurin can be synthesised from acetate, but this seems unlikely, because acetate is more efficiently utilised when aneurin is present. Growth is slow and erratic and the final population is only

TABLE II.

The Behaviour of the Strain with Alternative Sources of Carbon or Nitrogen.

Medium :	Mean generation time at standard aneurin concn. (mins.).	Stationary population at standard aneurin concn. (millions per ml.).	Stationary population when tested in aneurin-free medium (millions per ml.).
(*A*) $(NH_4)_2SO_4$ *plus* :			
Glucose	120	500	2·7
Glycerol	120	300	3·9
Lactate	300 (140)	100	3·6
Pyruvate	>500 (210)	30	4·3
Acetate	300 (150)	100	23·6
Citrate		Does not support growth	
Aconitate		Does not support growth	
α-Ketoglutarate		Does not support growth	
Succinate	220 (140)	130	3·7
Fumarate	190 (140)	50	3·1
Malate	220	40	1·7
Oxaloacetate		Does not support growth	
(*B*) *Glucose plus* :			
β-Alanine	270	400	3·2
Glutamate	120	550	4·1
Aspartate	150	480	4·7
Asparagine	110	1,300	2·6
Glycine	300	250	2·0
L-Leucine	170	580	2·5
Ammonium sulphate	120	500	2·7
26 Amino-acids	110	450	3·3

In the case of nutrients which support a faster growth rate after serial sub-culture than that attained when cells are first tested in the new medium, the initial mean generation time is listed, followed by the minimum generation time in parentheses.

25 million cells per ml. in the absence of aneurin, whereas in its presence the initial generation time is 300 minutes and the final population is 100 million cells per ml. It seems more probable that there are alternative routes for the oxidation of acetate, one of which is independent of aneurin. In the presence of aneurin, a more efficient route can be brought into action.

Although it is unlikely that the complex of metabolic processes occuring in living organisms can be precisely described in terms of a single scheme of reactions, there is no doubt that reaction cycles play an important part in such processes (cf. Krebs, *Enzymologia*, 1947, **12**, 88). The well-known tricarboxylic acid cycle (cf. Baldwin, " Dynamic Aspects of Biochemistry," Cambridge, 1947, Chapters XII and XIII; Ochoa, *Physiol. Rev.*, 1951, **31**, 56) may be taken as a guide to the mode of metabolism of carbon compounds and to the interpretation of the behaviour of our yeast strain in different carbon sources.

When our results are considered in this light, it seems reasonable to suppose that most substrates support growth only in the presence of aneurin because the latter is required as a catalyst in the oxidative decarboxylation of pyruvate (cf. Peters, *Nature*, 1940, **146**, 387). Acetate may be able to support growth in the absence of aneurin because it enters the scheme after this stage.

It is noticeable that citrate, aconitate, and α-ketoglutarate do not support growth, while succinate does. The proposal of a condensed cycle, in which acetate is directly oxidised to succinate, has received some support (cf. Weinhouse *et al.*, *J. Amer. Chem. Soc.*, 1948, **70**, 3680. It is conceivable that, in our strain, reactions of this type could occur instead of those involving tricarboxylic acids, which would thus fail to support growth.

The explanation of the comparative behaviour observed in succinate, fumarate, malate, oxaloacetate, acetate, and pyruvate cannot, however, be so simple. After training of the yeast, succinate, fumarate and acetate can support rapid growth, but growth in malate or pyruvate is much slower, and oxaloacetate does not support it at all.

The interpretation of these results in terms of reaction schemes cannot seriously be attempted until more evidence is available. The possible effects of different rates of penetration into the cell by different substrates have not been investigated. However, apart from them, the behaviour of our yeast strain in different substrates must be dependent on their relation to the possible modes of carbon metabolism.

One of the authors (S. J.) thanks the Brewing Industry Research Foundation for the opportunity to engage in this work.

THE PHYSICAL CHEMISTRY LABORATORY, OXFORD. [*Received, January 11th*, 1951.]

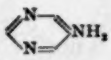
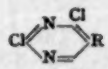
354. *A New Synthesis and the Chemical Properties of 5-Aminopyrimidine.*

By N. Whittaker.

[*With Physical Measurements* by T. S. G. Jones.]

Suitable conditions have been determined for the catalytic dechlorination of chloropyrimidines. 5-Aminopyrimidine (I) has been synthesised from uracil, *via* 5-amino-2 : 4-dichloropyrimidine (II; R = NH_2), in 44% over-all yield. The chemical and some physical properties of the former have been examined and a number of derivatives prepared. 5-Aminopyrimidine did not give a diazonium salt, but its dichloro-derivative was converted by nitrous acid into diazouracil (VII); the mechanism of this reaction is discussed.

During a recent study of derivatives of heterocyclic amines a quantity of 5-aminopyrimidine (I) was required. This substance had been synthesised by Roblin, Winnek, and English (*J. Amer. Chem. Soc.*, 1942, **64**, 567) from nitromalonic aldehyde by a five-stage process developed from the earlier work of Hale and Brill (*J. Amer. Chem. Soc.*, 1912, **34**, 82). For the preparation of 5-aminopyrimidine in quantity a simpler synthesis seemed desirable, and accordingly possible alternative routes were examined, one of which proved to be satisfactory.

(I.)   (II.)

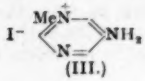
Uracil (2 : 4-dihydroxypyrimidine) was nitrated by a modification of Johnson's method (*J. Amer. Chem. Soc.*, 1919, **41**, 783) and the 5-nitrouracil thus produced was converted into 2 : 4-dichloro-5-nitropyrimidine (II; R = NO_2) in good yield (cf. Isay, *Ber.*, 1906, **39**, 252) by boiling phosphoryl chloride in the presence of dimethylaniline. The catalytic influence of dimethylaniline on the replacement of hydroxyl by chlorine in hydroxypyrimidines, which obviates the use of sealed tubes, has already been well exemplified (Kenner, Lythgoe, Todd, and Topham, *J.*, 1943, 575; Baddiley and Topham, *J.*, 1944, 678; King, King, and Spensley, *J.*, 1947, 1247), but examples are encountered where the method is not satisfactory. It was not possible to convert 5-nitrobarbituric acid into the corresponding trichloronitropyrimidine, but this might be the consequence of further reaction of the chloropyrimidine with the dimethylaniline (cf. Ross, *J.*, 1948, 1129; King *et al.*, *loc. cit.*). The chlorination of uracil by this method gave 2 : 4-dichloropyrimidine in excellent yield.

Ferrous hydroxide reduced 2 : 4-dichloro-5-nitropyrimidine (II; R = NO_2) to 5-amino-2 : 4-dichloropyrimidine (II; R = NH_2) in good yield. Before attempting the dechlorination of this substance experiments were first conducted with 2 : 4 : 6-trichloro- and 2 : 4-dichloropyrimidine. Aqueous-alcoholic suspensions of 2 : 4 : 6-trichloropyrimidine containing a palladium–charcoal catalyst were shaken with hydrogen at atmospheric pressure in the presence of various bases as hydrogen chloride acceptors. When the base was sodium carbonate some hydrolysis of reactive chlorine occurred and a low uptake of hydrogen was recorded. In the presence of sodium acetate, which gave a buffered solution of slightly acid pH, reduction of the pyrimidine ring occurred in addition to dechlorination with absorption of more than 5 mols. of hydrogen. With magnesium oxide, however, the theoretical uptake of 3 mols. was achieved. Similarly with 2 : 4-dichloropyrimidine in the presence of magnesium oxide, reaction ceased when 2 mols. of hydrogen had been absorbed, and pyrimidine was isolated, by precipitation as the mercuric chloride compound, in 92% yield. When this procedure was applied to 5-amino-2 : 4-dichloropyrimidine (II; R = NH_2), preferably in aqueous suspension, a magnesium chloride compound of 5-aminopyrimidine, and thence 5-aminopyrimidine, were isolated in good yield.

In an attempt to effect simultaneous reduction of the nitro-group and dechlorination of 2 : 4-dichloro-5-nitropyrimidine (II; R = NO_2) with palladium–charcoal and hydrogen under pressure, a colourless solution was obtained which did not contain 5-aminopyrimidine (cf. the similar finding by Roblin *et al.*, *loc. cit.*, with 2-chloro-5-nitropyrimidine). This solution was oxidised in the air to a water-soluble azo-product. The reduction of 2 : 4-dichloro-5-nitropyrimidine (II; R = NO_2) with zinc dust by the method used for the corresponding 6-methyl

compound (Gabriel and Colman, *Ber.*, 1901, **34**, 1250—1252) did not produce 5-amino-2-chloropyrimidine. 5-Amino-2 : 4-dimercaptopyrimidine, prepared from 2 : 4-dichloro-5-nitropyrimidine (II; R = NO_2) by reaction with sodium hydrogen sulphide, was heated under reflux in alkaline solution with a large excess of Raney nickel (Mozingo *et al.*, *J. Amer. Chem. Soc.*, 1943, **65**, 1013), but no 5-aminopyrimidine was isolated.

5-Aminopyrimidine formed colourless prisms, m. p. 171—172° (Roblin *et al.*, *loc. cit.*, give m. p. 170—171°). Molecular-weight determinations confirmed the mononuclear structure, so that the high melting point, and the low solubility in non-polar solvents, must be attributed to a strengthening of the crystal lattice by hydrogen-bonding between the amino-groups and the negatively charged ring-nitrogen atoms of adjacent molecules. 5-Aminopyrimidine is stable in the solid state or in aqueous solution, but the addition of mineral acid causes ready atmospheric oxidation with formation of dark amorphous material. The substance has only weak basic character, giving in concentrated aqueous solution a neutral (litmus) reaction, consistent with the pK_a value of 2·6 given in a later section. 5-Aminopyrimidine readily formed a methiodide (III) by reaction with cold methanolic methyl iodide. Bromine in aqueous solution converted 5-aminopyrimidine into an intractable black substance, and therefore further characterisation was sought by the preparation of derivatives with substituents on the amino-group rather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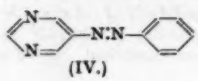
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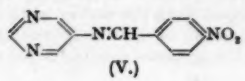
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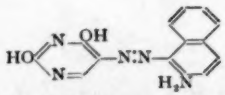
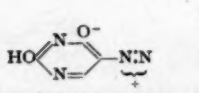
(VI.)



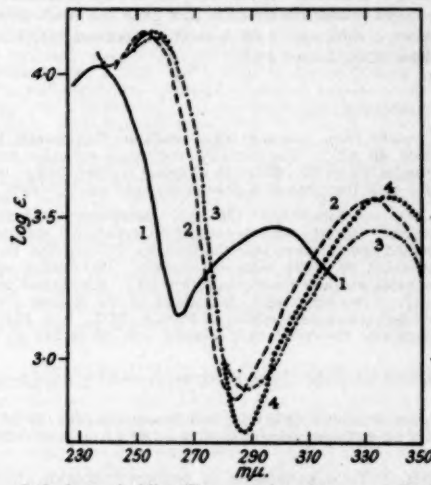

(VII.)

than by electrophilic substitution in the nucleus. 5-Acetamido- and 5-benzamido-pyrimidine were obtained by customary methods. The inherent low nucleophilic reactivity of the functional group of 5-aminopyrimidine was observed in the absence of reaction with nitrosobenzene under conditions which produce azobenzene from aniline and nitrosobenzene (Baeyer, *Ber.*, 1874, **7**, 1638). When the components were heated in acetic acid, however, 5-phenylazopyrimidine (IV) was obtained. Similarly, vigorous conditions were necessary to produce the Schiff's base 5-*p*-nitrobenzylideneaminopyrimidine (V). 5-Aminopyrimidine did not give a diazonium salt with nitrous acid or nitrosylsulphuric acid. In contrast, 5-amino-2 : 4-dichloropyrimidine (II; R = NH_2) formed a diazonium salt which could be coupled with β-naphthylamine in acid solution to give an azo-compound in the form of a purple hydrochloride. The new red base was shown to be 2-amino-1-(2 : 4-dihydroxy-5-pyrimidylazo)naphthalene (VI) by reduction with sodium dithionite to 1 : 2-diaminonaphthalene, which gave the characteristic 2 : 3-diphenyl-5 : 6-benzoquinoxaline with benzil. The possibility that the reagents used in the neutralisation of the purple hydrochloride had effected hydrolysis of some reactive chlorine in the pyrimidine nucleus was excluded by the fact that hot aqueous 2-hydroxyethylamine produced the same azo-compound (VI) and not a 2-hydroxyethylamino-derivative. In the reaction of 5-amino-2 : 4-dichloropyrimidine (II; R = NH_2) with nitrous acid, hydrolysis of both chlorine atoms had occurred simultaneously with diazotisation, and thus it was possible to effect diazotisation by using 0·5 molecular equivalent of hydrochloric acid per mole of sodium nitrite. The solution produced in this way had a characteristic instability to heat, but by neutralisation of the hydrochloric acid formed by hydrolysis, the known heat-stable diazouracil (VII) was produced (Behrend and Ernert, *Annalen*, 1890, **258**, 347; Johnson, Baudisch, and Hoffmann, *Ber.*, 1931, **64**, 2629; Bogert and Davidson, *Proc. Nat. Acad. Sci.*, 1932, **18**, 215). The representation (VII) is arbitrary since the precise structure of diazouracil has not yet been determined. It is now suggested that in acid solution an equilibrium exists between the dihydroxypyrimidinediazonium chloride and diazouracil, although strongly on the side of the latter; the former is the unstable compound which undergoes coupling. It is postulated that a combination of two factors is responsible for the production of a diazo-compound from 5-amino-2 : 4-dichloropyrimidine (II; R = NH_2) which are not operative with 5-aminopyrimidine: at the instant of reaction with nitrous acid the chlorine atoms of the transitional diazonium salt, activated by the exocyclic positive pole, are replaced by hydroxyl and rapid transformation into the stabilised zwitterion structure of diazouracil follows. If this explanation is correct the ability to form diazo-compounds may well be confined to those 5-aminopyrimidines with at

least one hydroxyl substituent, or a substituent capable of conversion into hydroxyl, *e.g.*, alkylthio- or alkoxy-, under the conditions of diazotisation.

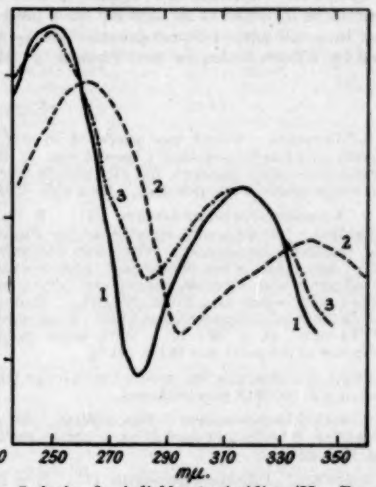
Physical Measurements.—Ultra-violet absorption spectra. Fig. 1 shows the ultra-violet absorption curves for 5-aminopyrimidine in solution in water and 0·1N-hydrochloric acid. The two peaks found in the former solvent are also present in the acid solution but both are shifted to longer wave-lengths, and the intensity of absorption is increased. Cation formation must therefore involve the attachment of a proton to one of the equivalent ring-nitrogen atoms rather than to the amino-group, since by Waterman's rule the spectrum of the 5-pyrimidyl-

FIG. 1.



5-Aminopyrimidine (I): —— *in water*, – – – – *in* 0·1N-HCl. *5-Amino-1-methylpyrimidinium iodide* (III): . . . . *in water*, – · – · – *in* 0·1N-HCl.

FIG. 2.



5-Amino-2:4-dichloropyrimidine (II; R = NH_2): —— *in water*, – – – – *in* 5N-HCl, – · – · – *in* 5N-HCl *subsequently neutralised by sodium acetate.*

ammonium ion should approximate to that of pyrimidine itself ($\lambda_{max.}$ 245 mμ.; $\varepsilon_{max.}$ = 3000; Heyroth and Loofbourow, *J. Amer. Chem. Soc.*, 1934, **56**, 1728). This interpretation is confirmed by the absorption curves of 5-aminopyrimidine methiodide (Fig. 1), the structure of which is known from its method of formation and chemical properties. The great similarity of the curves for this compound in acid and neutral solution with that of 5-aminopyrimidine in acid solution is evident. A small correction should be made for the absorption of the iodide ion in the region of 250 mμ., but would not significantly affect the course of the curves much above 260 mμ. 5-Aminopyrimidine is rapidly decomposed in 5N-hydrochloric acid. The band at

Name.	Medium.	λ (mμ.).	ε (max.).	λ (mμ.).	ε (max.).
5-Aminopyrimidine	Water	236	11,000	298	3,100
	0·1N-HCl	253	14,400	332	3,700
5-Amino-1-methylpyrimidinium iodide	Water	256	14,300	337	3,700
	0·1N-HCl	257	14,000	339	3,100
5-Amino-2:4-dichloropyrimidine	Water	250	15,100	316	4,100
	5N-HCl	265	9,700	340	2,700
	5N-HCl neutralised by sodium acetate	251	14,300	317	4,000
5-Benzamidopyrimidine	Water	256	17,500	—	—
	0·1N-HCl	262	20,900	—	—
	5N-HCl	265	26,400	—	—
5-Acetamidopyrimidine	Water	236	13,000	275 (inflexion)	2,800
5-Phenylazopyrimidine	10% EtOH in water	232	9,500	315	15,400
5-*p*-Nitrobenzylideneaminopyrimidine	EtOH	303	20,400	—	—

~250 mμ. is scarcely affected but that at ~330 mμ. progressively decreases in intensity and broadens.

5-Amino-2 : 4-dichloropyrimidine also takes up a proton on a ring-nitrogen atom in acid solution to give a spectrum with a corresponding shift in wave-length but a diminution in intensity, and differing from that of 2 : 4-dichloropyrimidine (Heyroth and Loofbourow, *loc. cit.*). In 5N-hydrochloric acid (Fig. 2) this compound is more stable than 5-aminopyrimidine, for, on its neutralisation with sodium acetate, the spectrum reverts to that of the neutral solution, although with a distinct change in the minimum.

Details for these and other compounds are collected in the Table.

Ionisation constant. The apparent dissociation constants of the conjugate acid of 5-aminopyrimidine in water at 25° and 40° have been found potentiometrically (the glass electrode being used in a cell with a liquid junction) to be 2·60 ± 0·01 and 2·62 ± 0·03 respectively (Roblin, cited by Albert, Goldacre, and Phillips, *J.*, 1948, 2246, found 2·83).

Experimental.

5-Nitrouracil.—Uracil was prepared in 92% yield from commercially available 2-thiouracil by Wheeler and Liddle's method (*Amer. Chem. J.*, 1908, **40**, 547). The initially exothermic nitration with fuming nitric acid (Johnson, *loc. cit.*) should be conducted at 60—65° with external cooling, before the final evaporation in an open dish. On a 150—200 g. scale the yield of 5-nitro-compound was 97—98%.

2 : 4-*Dichloro-5-nitropyrimidine* (II; R = NO_2).—5-Nitrouracil (26 g.), phosphoryl chloride (redistilled; 130 ml.), and dimethylaniline (redistilled; 32 ml.) were heated, with occasional shaking, until reaction commenced. When this had subsided the mixture was refluxed for 70 minutes, then cooled, and most of the phosphoryl chloride evaporated off under reduced pressure. The residue was poured on ice with vigorous stirring and, after 5 minutes, extracted with ether (500 ml.); the extract was washed with water and dried (Na_2SO_4). Removal of the ether and distillation of the residue gave 2 : 4-dichloro-5-nitropyrimidine which, when redistilled, was a pale yellow oil (23·0 g., 72%), b. p. 138—139°/14 mm., m. p. 29—30°. With larger preparations the yield was reduced, *e.g.*, from 214 g. of 5-nitrouracil the yield was 161 g. (61%).

Delay in extracting the product with ether reduced the yield; in an experiment with 16 hours' delay none of the product was obtained.

2 : 4-*Dichloropyrimidine.*—Uracil (50 g.), phosphoryl chloride (250 ml.), and dimethylaniline (62 ml.), refluxed for 2 hours and worked up as above, gave 2 : 4-dichloropyrimidine (57·6 g., 87%), m. p. 61—62°, b. p. 100°/22 mm.

5-*Amino*-2 : 4-*dichloropyrimidine* (II; R = NH_2).—To a suspension of ferrous hydroxide (from ferrous sulphate heptahydrate, 516 g., and barium hydroxide octahydrate, 586 g., in hot water, 6 l.) at 70—75°, molten 2 : 4-dichloro-5-nitropyrimidine (40 g.) was added with powerful stirring, and the temperature quickly raised to 90—95°. Reduction was rapid, and, after 30 minutes' heating, the mixture was filtered hot and the black residue washed with hot water. The aqueous liquors were concentrated *in vacuo* to *ca.* 1·5 l., the crystalline product was collected, and the mother-liquor extracted with chloroform (2 × 400 ml.). After being dried (Na_2SO_4) the extract was evaporated, and the combined product sublimed (110—115°/2 mm.) to give colourless dense prisms, which were recrystallised from benzene–light petroleum (80—100°). 5-*Amino*-2 : 4-*dichloropyrimidine* (27·6 g., 82%) was thus obtained in colourless needles, m. p. 121·5—122·5° (Found: C, 29·55; H, 2·0; N, 25·55; Cl, 42·75. $C_4H_3N_3Cl_2$ requires C, 29·3; H, 1·85; N, 25·6; Cl, 43·3%).

Catalytic Dechlorination of Chloropyrimidines.—The volumes quoted below are at N.T.P. A palladium–charcoal catalyst (*ca.* 3% of Pd) was used throughout, 1 g. requiring 30 ml. hydrogen for saturation.

(*a*) A mixture of 2 : 4 : 6-trichloropyrimidine 2 g.) (Baddiley and Topham, *loc. cit.*), magnesium oxide (2 g.), catalyst (0·5 g.), alcohol (20 ml.), and water (60 ml.) was shaken with hydrogen at one atmosphere. Absorption ceased after 190 minutes when 765 ml. of hydrogen had been utilised (2nd expt., 783 ml.; calc., 747 ml.).

(*b*) When 2 : 4-dichloropyrimidine (15 g.), magnesium oxide (15 g.), catalyst (4 g.), alcohol (75 ml.), and water (150 ml.) were treated as in (*a*), absorption of hydrogen (4710 ml.; calc., 4635 ml.) was complete after 155 minutes. The mixture was then filtered, the residue was washed with water, and the combined filtrates were steam-distilled until the distillate gave no further precipitate with aqueous mercuric chloride. The total distillate was treated with an excess of mercuric chloride solution; pyrimidine mercurichloride ($C_4H_4N_2,HgCl_2$) was thus obtained (32·4 g., 92%).

(*c*) A mixture of 5-amino-2 : 4-dichloropyrimidine (6 g.), magnesium oxide (6 g.), catalyst (6 g.), and water (150 ml.) absorbed 1940 ml. hydrogen during 190 minutes (calc., 1820 ml.). After filtration the residue was washed with water, and the combined filtrates were evaporated to dryness *in vacuo*. The magnesium chloride compound of 5-aminopyrimidine thus left was dried, and then dissolved in warm alcohol (150 ml.) and poured through a column of activated alumina (200 g.). The column was washed with alcohol, and the colourless eluate evaporated to leave a residue of 5-aminopyrimidine, which crystallised from benzene, forming first colourless needles but later prisms (2·66 g., 77%), m. p. 171—172° with sublimation [Found: C, 50·95; H, 4·7; N, 44·05; *M* (Rast; camphor), 90, 110. Calc. for $C_4H_5N_3$: C, 50·55; H, 5·25; N, 44·2%; *M*, 95].

When the dechlorination was effected in 50% aqueous alcohol a further 30 minutes was required, but in alcoholic solution reaction was incomplete after 5 hours.

5-Amino-2 : 4-dimercaptopyrimidine.—To a solution of sodium hydrogen sulphide, prepared by saturating a solution of sodium (5 g.) in alcohol (100 ml.) and water (30 ml.) at room temperature with hydrogen sulphide, a solution of 2 : 4-dichloro-5-nitropyrimidine (5 g.) in alcohol (15 ml.) was added dropwise with shaking. The mixture was refluxed for 2 hours, cooled, diluted with water, and acidified with acetic acid. When the solvent had been evaporated *in vacuo*, the residue was suspended in water (500 ml.), and sufficient sodium carbonate solution added to dissolve the product. Sulphur was removed by filtration and the filtrate acidified with acetic acid to precipitate *5-amino-2 : 4-dimercaptopyrimidine* (3·5 g.). This substance dissolved in hot water to give a pale yellow solution from which brown needles, yellow in transmitted light, separated on cooling, but it was unstable to prolonged heating with water. It darkened above 220° and decomposed at *ca.* 270° with evolution of hydrogen sulphide (Found : C, 31·1; H, 2·9; N, 26·2; S, 40·25. $C_4H_4N_3S_2$ requires C, 30·2; H, 3·15; N, 26·4; S, 40·25%).

5-Amino-1-methylpyrimidinium Iodide (III).—A solution of 5-aminopyrimidine (0·5 g.) in methanol (5 ml.) was treated with methyl iodide (1 ml.) and after 72 hours the crystalline product (0·64 g.) was collected (m. p. 166—167°) (mother-liquors yielded a further 0·29 g.) and recrystallised from alcohol. The *methiodide* was obtained as prisms, yellow-brown in reflected light and pale yellow in transmitted light, m. p. 166—167°. A powdered specimen was colourless (Found : C, 25·75; H, 3·5; N, 17·55; I, 53·7. $C_5H_8N_3I$ requires C, 25·3; H, 3·4; N, 17·7; I, 53·6%). The product dissolved readily in water to give a neutral (litmus) solution.

5-Acetamidopyrimidine.—5-Aminopyrimidine (0·25 g.), acetic anhydride (1 ml.), and benzene (5 ml.) were refluxed for 2 hours. On cooling, *5-acetamidopyrimidine* separated as colourless prisms, m. p. 147—149°, raised by recrystallisation from benzene to 148—149° (Found : C, 53·1; H, 5·0; N, 31·15. $C_6H_7ON_3$ requires C, 52·55; H, 5·1; N, 30·65%).

5-Benzamidopyrimidine.—Benzoyl chloride (3·3 ml.) was added to a solution of 5-aminopyrimidine (2 g.) in dry pyridine (20 ml.) and the reaction liquid left overnight. The pyridine was evaporated *in vacuo* and the residue shaken with chloroform (*ca.* 200 ml.) and water (50 ml.). The chloroform layer was separated, washed once with water, and evaporated. The residual solid was purified by recrystallisation from water (some dark residue), and then from benzene, to give *5-benzamidopyrimidine* as colourless prisms (2·5 g.), m. p. 146—147° (Found : C, 66·55; H, 4·5; N, 21·3. $C_{11}H_9ON_3$ requires C, 66·35; H, 4·5; N, 21·1%).

5-Phenylazopyrimidine (IV).—A mixture of 5-aminopyrimidine (0·5 g.), nitrosobenzene (0·6 g.), and glacial acetic acid (6 ml.) was refluxed for 2½ hours. The solvent was evaporated *in vacuo* and the dark residue digested with hot water and evaporated once more. A chloroform extract of the residue was washed with water, dried (Na_2SO_4), and chromatographed (Al_2O_3), the column being developed with chloroform. A diffuse yellow-orange band descended the column to yield an orange eluate, from which the chloroform was evaporated, and the residual material purified by further chromatography (Al_2O_3) in benzene and then by recrystallisation from light petroleum (b. p. 60—80°). *5-Phenylazopyrimidine* was thus obtained as red plates (0·1 g.), m. p. 97·5—98° (Found : C, 65·3; H, 4·45; N, 30·05. $C_{10}H_8N_4$ requires C, 65·2; H, 4·35; N, 30·45%); it was sparingly soluble in hot water, from which fine orange needles separated on cooling.

5-p-Nitrobenzylideneaminopyrimidine (V) was the product of heating 5-aminopyrimidine (50 mg.), *p*-nitrobenzaldehyde (75 mg.), and glacial acetic acid (0·1 ml.) at 160° for 5 minutes. After cooling, the solid product was ground under water and collected (110 mg.), m. p. 185—186°. By recrystallisation from alcohol the sparingly soluble product was obtained in fine yellow needles, unchanged in m. p. (Found : C, 57·7; H, 3·35; N, 24·7. $C_{11}H_8O_2N_4$ requires C, 57·9; H, 3·5; N, 24·55%).

Reactions with Nitrous Acid.—(a) *5-Aminopyrimidine.* To an ice-cooled solution of 5-aminopyrimidine (0·25 g.), in water (6 ml.) and concentrated hydrochloric acid (0·8 ml.), under carbon dioxide, a solution of sodium nitrite (0·19 g.) in water (2 ml.) was added drop-wise. Vigorous evolution of gas occurred immediately. After 5 minutes the liberated gases were swept by a current of carbon dioxide through a U-tube containing ferrous sulphate-impregnated pumice, and the nitrogen collected in a nitrometer over 50% aqueous potassium hydroxide. The volume of nitrogen collected (45·4 ml.; 45·2 ml. at N.T.P.) corresponded to 77% conversion of amino-group into nitrogen. The same reaction at −5° gave 43·4 ml. nitrogen.

(b) *5-Amino-2 : 4-dichloropyrimidine* (II; R = NH_2). A solution of 5-amino-2 : 4-dichloropyrimidine (1 g., 1 mol.) in hot water (15 ml.) was cooled quickly to 0°, and 10N-hydrochloric acid (2 ml., 3·3 mols.) added to the suspension of fine needles thus produced. A cold solution of sodium nitrite (0·41 g., 1 mol.) in water (4 ml.) was then added quickly with shaking and cooling. After 2 minutes the nitrous acid-free, clear solution was poured into a solution prepared by heating β-naphthylamine (1 g.), water (40 ml.), and 10N-hydrochloric acid (1 ml.) and rapid cooling to 0°. The mixture was shaken at 0° for 1 hour, and the purple crystalline precipitate collected, and washed with 0·1N-hydrochloric acid and then with water. This substance was heated for a few minutes with dilute aqueous sodium hydroxide or sodium acetate containing 10% of alcohol, acidified with acetic acid, and cooled. The red solid (0·98 g.), m. p. 264—265° (decomp.), was purified by chromatography (Al_2O_3) in pyridine, the product being eluted with pyridine–methanol–water. The solvent was evaporated from the eluate, and the residual solid digested with aqueous acetic acid and cooled. Recrystallised from 2-ethoxyethanol it gave red plates and prisms of *2-amino-1-(2 : 4-dihydroxy-5-pyrimidylazo)naphthalene* (VI), m. p. 269—270° (decomp.) (Found : C, 59·55; H, 3·9; N, 25·0. $C_{14}H_{11}O_2N_5$ requires C, 59·8; H, 3·9; N, 24·9%). Crude (VI) (1·95 g.) was suspended in hot aqueous sodium hydroxide and reduced with sodium dithionite. When the solid had dissolved the liquid was filtered, cooled and extracted with ether. The extract was washed with water, dried (Na_2SO_4), and evaporated in a stream of nitrogen.

To the residual 1 : 2-diaminonaphthalene thus obtained, benzil (1·45 g.), alcohol (20 ml.), and concentrated hydrochloric acid (0·1 ml.) were added. The mixture was refluxed for 1 hour, cooled, and diluted with water, and the precipitated solid thrice recrystallised from alcohol to give 2 : 3-diphenyl-5 : 6-benzoquinoxaline as straw-coloured prisms (0·9 g.), m. p. 148—149° (Found: C, 86·65; H, 4·9; N, 8·7. Calc. for $C_{24}H_{16}N_2$: C, 86·75; H, 4·8; N, 8·45%). Lawson (*Ber.*, 1885, **18**, 2426) gives m. p. 147°.

When 5-amino-2 : 4-dichloropyrimidine (1 g., 1 mol.) was diazotised in the presence of 0·3 ml. (0·5 mol.) of 10N-hydrochloric acid, a clear solution was also obtained. Evolution of nitrogen was slight at 0°, but with heating this became vigorous and a yellow-brown solid separated. When the acid (1·5 mols.) was neutralised by magnesium oxide or aqueous ammonia the solution was stable to heat, and by concentration *in vacuo* diazouracil was isolated as an amorphous yellow solid. The neutralised solution coupled slowly with β-naphthol (Bogert and Davidson, *loc. cit.*).

Physical Determinations.—Absorption spectra. These were determined photographically, the Hilger Medium Quartz Spectrograph and Spekker Photometer being used. Solutions were made up from weighed quantities of the materials in volumetric flasks.

Ionisation constants. Weighed quantities of 5-aminopyrimidine (0·5 m.-mol., 47·5 mg.) were dissolved in 5·00 ml. of conductivity water and titrated with 1·00M-HCl in a cell containing a glass electrode, calibrated by means of the phthalate, borate, and tetroxalate buffers recommended by Bates, Pinching, and Smith (*J. Res. Nat. Bur. Stand.*, 1950, **45**, 418). The solution was stirred by a current of nitrogen of suitable humidity. The reference electrode was a large calomel half-cell containing 3·5M-KCl and connected by a capillary bridge of 3·5M-KCl. The thermostat was maintained at 40° ± 0·1° or 25° ± 0·1°. Potentials were measured by using an electrometer tetrode as null indicator, the difference in potential of the electrode train and a Tinsley precision potentiometer being applied to the control grid. Potentials were reproducible to 0·1 mv. The titrant was admitted from a micrometer syringe, about thirty small additions being made. The pH values calculated from the potentials were plotted against the volume of titrant to give a smooth curve. The pK_a' values were then calculated from convenient points on the curve according to the equation, $pK_a' = pH - \log\{([B] + [H^+])/([BH^+] - [H^+])\}$, where [B], [BH⁺], and [H⁺] are the calculated concentrations of the base, conjugate acid, and hydrogen ion, corrected for the dilution caused by addition of acid but not for the activity coefficients.

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355. *An Investigation of the Course of the Reformatsky Reaction.*

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Evidence additional to that adduced by Dain (*J. Russ. Phys. Chem. Soc.*, 1896, **28**, 593) has been provided for the production of intermediate compounds in the course of the Reformatsky synthesis of β-hydroxy-esters. Solid products have been isolated which have been shown to be derived from the components zinc, α-halogeno-ester, and ketone or aldehyde. The product which is deposited after the interaction of zinc and the α-halogeno-ester alone is now regarded as formed by self-condensation of the transitory primary intermediate product. This may be precipitated alongside the secondary intermediate product, and so, after hydrolysis, yield a β-ketonic ester as impurity in the final product of the synthesis.

IN the Reformatsky reaction an α-halogeno-carboxylic ester, usually the bromo-ester, is condensed with an aldehyde or ketone, in the presence of zinc, to give a β-hydroxy-ester. The reaction is carried out in two stages: first, the reactants are refluxed in a non-hydroxylic solvent and then the product is hydrolysed by cold dilute acid. Reformatsky (*J. pr. Chem.*, 1896, **54**, 469) postulated a course whereby the α-halogeno-ester forms, with the zinc, a primary intermediate (I), which with the aldehyde or ketone forms a secondary intermediate (II), which can be hydrolysed to the β-hydroxy-ester:

$$Br{\cdot}CHR{\cdot}CO_2Et + Zn \longrightarrow BrZn{\cdot}CHR{\cdot}CO_2Et \quad (I.)$$

$$>CO + (I) \longrightarrow >C(O{\cdot}ZnBr){\cdot}CHR{\cdot}CO_2Et \xrightarrow[HCl]{Dil.} >C(OH){\cdot}CHR{\cdot}CO_2Et + ZnClBr$$

(II.)

Experimental confirmation was obtained by Dain (*J. Russ. Phys. Chem. Soc.*, 1896, **28**, 543) who isolated a yellow solid from a mixture of zinc and ethyl α-bromo*iso*butyrate which gave a

bromine analysis in fair agreement with the formula (I). Comparable results were obtained with zinc and ethyl α-bromo*iso*valerate, but no other tests were carried out to prove the identity of these solids.

From a mixture of zinc, benzaldehyde, and ethyl α-bromopropionate Dain isolated a yellow solid giving a bromine analysis which signified a secondary intermediate (II), the identity being confirmed by hydrolysis with dilute acid to the expected β-hydroxy-ester. Similar observations were made when using the α-bromo-*iso*butyrate and -*iso*valerate.

Little further investigation has since been made of the solids formed during Reformatsky reactions although their occurrence has been mentioned incidentally by several workers. The widely varying yields from case to case and the unreactivity of certain ketones in the reaction have led to studies of the by-products. Hann and Lapworth (*Proc. Chem. Soc.*, 1903, **19**, 189) claimed to have isolated ethyl γ-bromoacetoacetate from reactions employing ethyl bromoacetate, and presumed it to be formed by the action of the primary intermediate on the carbethoxyl group of unchanged bromo-ester. This observation was not confirmed by Hussey and Newman (*J. Amer. Chem. Soc.*, 1948, **70**, 3024) who, nevertheless, isolated unhalogenated β-ketonic carboxylic esters, and simple esters (the reduced α-bromo-esters), from reactions with and without a ketone. Zeltner (*Ber.*, 1908, **41**, 589; *J. pr. Chem.*, 1908, **78**, 97) found that where the zinc was replaced by magnesium no β-hydroxy-esters were formed : instead, reduced esters and β-ketonic esters were isolated. The β-ketonic esters were considered by Zeltner to be formed by the condensation of two molecules comparable with Reformatsky's primary intermediate (I). Hussey and Newman (*loc. cit.*) offer a less convincing explanation of the production of β-ketonic esters, and the formation of the reduced ester is considered to arise from a reaction of the enolic form of the ketone (cf. Newman, *J. Amer. Chem. Soc.*, 1940, **62**, 870; 1942, **64**, 2131), a view which is however inconsistent with facts such as the formation of methyl crotonate in the Reformatsky reaction involving methyl γ-bromocrotonate and benzaldehyde (Jones, O'Sullivan, and Whiting, *J.*, 1949, 1415).

The purpose of our investigation was to determine afresh the composition of the solid deposits which separate in Reformatsky reactions and, also, to ascertain whether they are truly intermediates.

A boiling mixture of benzophenone, ethyl bromoacetate, and zinc in benzene deposited a yellow solid, zinc and bromine analyses of which indicated a formula $BrZn{\cdot}O{\cdot}CPh_2{\cdot}CH_2{\cdot}CO_2Et$, *i.e.*, a secondary intermediate of Reformatsky's type (II) (see Table). This solid gave an almost quantitative yield of the appropriate β-hydroxy-ester, whereas no trace of such an ester could be isolated from the remainder of the reaction mixture, and it thus appears to be a true intermediate.

No solid separated from a boiling mixture of benzaldehyde, ethyl α-bromopropionate, and zinc in benzene, although an unsatisfactory deposit was produced on addition of light petroleum (b. p. 60—80°). A stable yellow solid was eventually obtained from these reactants on three months' storage without a solvent, and the zinc and bromine analyses of the product agreed well with formula (II). Experience with benzaldehyde, ethyl bromoacetate, and zinc was similar; although this solid gave, after hydrolysis, cinnamic acid as expected, analyses were not as satisfactory as in the previous cases owing to contamination with metallic zinc.

Benzophenone and ethyl α-bromopropionate (unlike benzophenone and ethyl bromoacetate) failed to give a deposit when refluxed with zinc in benzene but yielded a pale yellow solid when

Ester,	CO-compound.	Formula of expected product.	Found, %. Zn.	Br.	Required, %. Zn.	Br.
$CH_2Br{\cdot}CO_2Et$	$COPh_2$	$C_{17}H_{17}O_3BrZn$	15·7	19·1	15·8	19·3
,, ...	Ph·CHO	$C_{11}H_{13}O_3BrZn$	21·5	20·6	19·3	23·6
,, ...	COPhMe	$C_{12}H_{15}O_3BrZn$	21·3	26·0	18·6	22·7
,, ...	*cyclo*Hexanone	$C_{10}H_{17}O_3BrZn$	22·5	27·2	19·7	24·2
$CHMeBr{\cdot}CO_2Et$	Ph·CHO	$C_{12}H_{15}O_3BrZn$	18·7	22·6	18·6	22·7
,, (2 expts.)	$COPh_2$	$C_{18}H_{19}O_3BrZn$	18·2, 18·7	22·5, 21·6	15·3	18·7

this solution was diluted with light petroleum. This compound, when treated with cold dilute acid, yielded the appropriate ethyl β-hydroxy-ββ-diphenyl*iso*butyrate, but the analyses for *both* zinc and bromine were high. Acetophenone or *cyclo*hexanone with ethyl bromoacetate and zinc yielded similar " impure " solid intermediates (see Table). The reason for these high analyses became apparent when the condensation of 1-benzoylnaphthalene with ethyl α-bromopropionate was attempted. When these two components were heated with zinc in benzene the metal dissolved but after hydrolysis about 90% of the initial ketone was recovered. In a similar

experiment the solid which separated during reaction was isolated and found to contain about twice the amount of bromine required for the secondary intermediate (II). Further, the same solid was obtained from a reaction in which the ketone was omitted, and when treated with dilute acid, it yields the β-ketonic ester, ethyl α-propionylpropionate. The most obvious explanation is the condensation of two molecules of the primary intermediate (I) (cf. Zeltner, *loc. cit.*, who suggested that similar compounds are produced in the reaction of magnesium with a bromo-ester):

$$2CH_3\cdot\underset{\underset{ZnBr}{|}}{CH}\cdot CO_2Et \longrightarrow \underset{\underset{ZnBr}{|}}{CH_3\cdot CH}\!\!-\!\!\underset{\underset{O\cdot ZnBr}{|}}{C(OEt)}\cdot CHMe\cdot CO_2Et \xrightarrow{2HCl} CH_3\cdot CH_2\cdot CO\cdot CHMe\cdot CO_2Et + 2ZnClBr + EtOH$$

(III.)

Analyses for the intermediate (two samples; Found: Zn, 27·1, 27·9; Br, 31·8, 30·8. $C_{16}H_{18}O_4Br_2Zn_2$ requires Zn, 26·5; Br, 32·4%) agree with the suggested formula (III) if contamination with a little metallic zinc is postulated.

Attempts to produce a β-ketonic ester complex from ethyl bromoacetate and zinc have, so far, only yielded tars, although the existence of such a complex is highly probable since Hussey and Newman (*loc. cit.*) have isolated ethyl acetoacetate from appropriate Reformatsky reactions. Moreover, we have been able to isolate ethyl α-*iso*butyryl*iso*butyrate after hydrolysis of the solid product deposited when zinc reacts with ethyl α-bromo*iso*butyrate, and also the solid analysed correctly.

The formation of these β-ketonic ester complexes explains the high zinc and bromine contents of some of the isolated β-hydroxy-ester complexes. Co-precipitation of the former complex with the latter will cause both the zinc and the bromine content of the resultant deposit to exceed those theoretically required by the pure β-hydroxy-ester complex. Purification by crystallisation has not been possible, owing to the insolubility in suitably inert solvents. It is true that some of these complexes have been isolated by precipitation from apparent solution in benzene but it is thought that these are very fine suspensions rather than true solutions.

The β-ketonic ester complexes were isolated by us by the method employed by Dain for his so-called "primary intermediates" (I). It is reasonably certain, therefore, that Dain's compounds were the β-ketonic ester complexes analogous to (III).

We believe, therefore, that the primary intermediate is soluble and has a rather transitory existence, and that the reactions involved are:

$$R\cdot CHBr\cdot CO_2Et + Zn \rightleftharpoons BrZn\cdot CHR\cdot CO_2Et \quad (I.)$$

$$BrZn\cdot CHR\cdot CO_2Et \xrightarrow{R_2CO} \underset{(IIa.)}{BrZn\cdot O\cdot CR_2\cdot CHR\cdot CO_2Et} \quad (A)$$

$$\downarrow BrZn\cdot CHR\cdot CO_2Et$$

$$\underset{\underset{ZnBr}{|}}{CHR}\!\!-\!\!\underset{\underset{O\cdot ZnBr}{|}}{C(OEt)}\cdot CHR\cdot CO_2Et \quad (IIIa.) \quad (B)$$

$$(IIa) \xrightarrow{HX} HO\cdot CR_2\cdot CHR\cdot CO_2Et + ZnBrX$$

$$(IIIa) \xrightarrow{2HX} CH_2R\cdot CO\cdot CHR\cdot CO_2Et + 2ZnBrX + EtOH$$

The amount of β-ketonic ester formed as a by-product will depend on the relative rates of the competing processes (*A*) and (*B*); if a sterically hindered ketone is used, *e.g.*, 1-benzoylnaphthalene, the reaction (*B*) may be dominant [in some cases Hussey and Newman (*loc. cit.*) have shown that the main product can be the β-ketonic ester]. Also, the complex (III*a*) may react further with the ester, and thus lead to the tars produced in many Reformatsky reactions.

The formation of reduced esters is explained by the above scheme as caused by hydrolysis of the primary intermediate (I) which has not undergone reaction (*A*) or (*B*).

Experimental.

Reformatsky reactions were conducted, and solid intermediate products separated, as described below; the procedures varied in detail, although 0·1 molar quantities of the organic reactants were generally employed and 0·1 atomic proportion of zinc.

The α-bromo-esters and liquid aldehydes and ketones were dried and distilled before use. The zinc foil or shavings were freshly cleaned by successive washings with 2·5% hydrochloric acid, distilled water,

alcohol, and ether, and dried for 1 hour at 100°. In the condensations where a solvent was employed the initial reaction was allowed to subside before the whole was refluxed on a steam-bath.

Benzophenone and Ethyl Bromoacetate.—Benzophenone (18·2 g.), ethyl bromoacetate (16·5 g.), and zinc (6·5 g.) were heated in a mixture of benzene (40 ml.) and toluene (35 ml.). Reaction occurred with some vigour and almost all the zinc dissolved in 2 hours; a solid gradually separated during the reaction. When the mixture had cooled the supernatant liquid was removed by means of a filter-tube, and the residual solid washed several times with dry benzene. Finally the pale yellow solid was removed as a suspension in benzene, recovered on a sintered-glass filter, and dried in a vacuum-desiccator, the whole operation being conducted in dry air (for analysis see Table).

This solid (5·2 g.) gave ethyl β-hydroxy-ββ-diphenylpropionate (3·3 g., 97%).

Benzophenone and Ethyl α-Bromopropionate.—Benzophenone (18·2 g.), ethyl α-bromopropionate (18·2 g.), and zinc (6·5 g.) were refluxed in benzene (25 ml.) for 1½ hours. The bulk of the zinc dissolved, leaving a clear liquid which was passed through a sintered-glass filter and poured slowly into light petroleum (b. p. 60—80°) (30 ml.). A white solid separated which was washed with further light petroleum and dried in a vacuum-desiccator (for analysis see Table).

Hydrolysis with 2N-sulphuric acid gave ethyl β-hydroxy-ββ-diphenyl*iso*butyrate.

Benzaldehyde and Ethyl Bromoacetate.—Benzaldehyde (10·6 g.), ethyl bromoacetate (16·5 g.), and zinc (6 g.), in a flask closed with a cork and wax, were kept at 0° for 12 hours and then at room temperature for 18 months, whereafter they comprised a yellow paste and a little unchanged zinc. Addition of benzene (10 ml.) produced a thick yellow suspension capable of being poured from the residual zinc. Further dilution of this liquid with benzene produced a yellow viscous material, but by addition of light petroleum (b. p. 60—80°) to this, a few ml. at a time, a pale yellow solid was obtained which was filtered off and washed with further light petroleum in a current of dry air (for analysis see Table).

Treatment first with 2N-sulphuric acid and then with 10% aqueous potassium hydroxide yielded cinnamic acid.

Benzaldehyde and Ethyl α-Bromopropionate.—Benzaldehyde (10·6 g.), ethyl α-bromopropionate (18·2 g.), and zinc (6·5 g.) were heated for 1 hour in benzene (30 ml.). A brisk reaction occurred and most of the zinc dissolved, to give a clear liquid from which no solid settled. This liquid was passed through a sintered-glass filter and poured slowly into light petroleum (b. p. 60—80°) (30 ml.), whereupon a deep yellow solid separated which, however, decomposed in a few minutes although out of contact with moist air.

The same quantities of reactants, in the absence of the solvent, were then set aside as in the case of benzaldehyde and ethyl bromoacetate; after 3 months all of the zinc had been digested. The resultant yellow paste was diluted with anhydrous ether, and on addition of light petroleum (b. p. 60—80°) a pale yellow solid was recovered (for analysis see Table).

Acetophenone and Ethyl Bromoacetate.—Acetophenone (12 g.), ethyl bromoacetate (16·5 g.), and zinc (6 g.) in benzene (40 ml.) were refluxed; the reaction proceeded with some vigour. Most of the zinc dissolved, leaving a deep-orange liquid which was decanted from unchanged zinc and poured into ether (40 ml.), giving a suspension from which an orange-coloured solid was precipitated by light petroleum (b. p. 60—80°) (40 ml.): this was washed with ether and dried in a vacuum-desiccator (for analysis see Table).

cyclo*Hexanone and Ethyl Bromoacetate.*—*cyclo*Hexanone (9·8 g.), ethyl bromoacetate (16·5 g.), and zinc (6·5 g.) in benzene (50 ml.) were refluxed for 3 hours. After a brisk reaction a white opalescent liquid was left which on addition of light petroleum (b. p. 60—80°) deposited a white solid (for analysis see Table).

1-*Benzoylnaphthalene and Ethyl α-Bromopropionate.*—1-Benzoylnaphthalene (4 g.), ethyl α-bromopropionate (3 g.), and zinc (1·1 g.) in benzene (20 ml.) were refluxed; all the zinc dissolved and a dark orange-coloured liquid remained which was treated with cold 2N-sulphuric acid. From the solid product, *ca.* 3·5 g. of the original ketone were alone recovered.

In a similar experiment an intermediate yellow solid was isolated [Found: Br, 29·8. Calc. for $C_{11}H_{11}O_3BrZn$ (intermediate of type II): Br, 16·7%].

Ethyl α-Bromopropionate and Zinc.—Ethyl α-bromopropionate (36 g.), zinc (13 g.), and benzene (50 ml.) were refluxed for 3 hours, most of the zinc dissolving and leaving an orange-coloured liquid. The liquid was diluted with dry ether (50 ml.); on addition of light petroleum (b. p. 60—80°) a yellow solid was deposited (for analyses see p. 1572).

This solid, hydrolysed with cold 2N-sulphuric acid, gave ethyl α-propionylpropionate, b. p. 200° (Hellon and Oppenheim, *Ber.*, 1877, **10**, 700, give b. p. 199°) (Found: C, 60·3; H, 8·7. Calc. for $C_8H_{14}O_3$: C, 60·7; H, 8·8%).

This ester (5 g.) was converted into the phenylpyrazolone derivative, m. p. (after recrystallisation from 5% alcohol) 108—110° (Hussey and Newman, *loc. cit.*, for 3-ethyl-4-methyl-1-phenyl-5-pyrazolone give m. p. 111°).

*Ethyl α-Bromo*iso*butyrate and Zinc.*—Ethyl α-bromo*iso*butyrate (100 g.), zinc (32·5 g.), and benzene (200 ml.) were refluxed for 2 hours, whereupon all the zinc seemed to have become digested, leaving a pale yellow opalescent liquid from which a pale yellow solid was precipitated by an equal volume of anhydrous ether (Found: Zn, 30·1; Br, 32·8. $C_{12}H_{22}O_4Br_2Zn_2$ requires Zn, 25·1; Br, 30·7%). A similar solid obtained from a mixture of the α-bromo-ester and zinc which had been set aside at room temperature for several months gave on analysis: Zn, 30·4; Br, 33·0%.

This solid, with 2N-sulphuric acid, yielded ethyl α-*iso*butyryl*iso*butyrate, b. p. 200° (Zeltner, *loc. cit.*, gives b. p. 202—203°) (Found: C, 63·1; H, 9·2. Calc. for $C_{10}H_{18}O_3$: C, 64·5; H, 9·7%).

Analyses.—Determinations of zinc and bromine were conducted as follows:

Zinc. The solid was incinerated to zinc oxide (the method used by Dain); or, better, the material was dissolved in acid, and (i) the solution titrated against standard potassium ferrocyanide, with diphenylbenzidine as an indicator, or (ii) the zinc was precipitated as zinc ammonium phosphate and converted into pyrophosphate. The last method was found the most reliable.

Bromine. The solid was dissolved in dilute nitric acid (10%), and the bromine determined by Volhard's method.

Other analyses were conducted by Drs. Weiler and Strauss.

The authors acknowledge the collaboration of Dr. H. K. Dean in the early stages of this investigation.

CHELSEA POLYTECHNIC, LONDON, S.W.3. [*Received, February 8th*, 1951.]

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356. *Ferric Thiocyanate. Part II.* The Distribution of Ferric Thiocyanate between Ether and Water.*

By J. Y. MACDONALD, K. M. MITCHELL, and A. T. S. MITCHELL.

The distribution of ferric thiocyanate between ether and water has been used to investigate the equilibrium between the various complexes. All complexes from $FeCNS^{2+}$ to $Fe(CNS)_6^{3-}$ have been shown to occur, and the mass-action constants of all except the neutral molecule been determined. The factor limiting accuracy seems to be the change of activity coefficient with composition, which occurs at high concentration even at constant ionic strength. Bjerrum's relationship, K_2/K_1, etc. = const., holds to a first approximation.

THE object of this work is to determine the nature of the complexes responsible for the colour in solutions of ferric thiocyanate. Migration experiments (*e.g.*, Schlesinger, *J. Amer. Chem. Soc.*, 1941, **63**, 1765; Bent and French, *ibid.*, p. 568) show that under suitable conditions either positively or negatively charged complexes may exist; and the fact that ether, amyl alcohol, and other solvents can extract the red colour from such solutions indicates the presence of a neutral complex which molecular-weight experiments (Part I *) show to have a formula $Fe(CNS)_3$ (for simplicity, the co-ordinated water molecules will be omitted in this discussion). A number of workers (references given in Part I) have proved the existence of the complex $FeCNS^{2+}$ in dilute solution, and have found some evidence of higher complexes in more concentrated solutions. The possibility of a complex $Fe(CNS)_6^{3-}$ is indicated both by analogy with the ferricyanides and by the existence of crystalline compounds of the type $M_3Fe(CNS)_6$ (Rosenheim and Cohn, *Z. anorg. Chem.*, 1901, **27**, 280).

In this work the possibility will be assumed that there exists a series of complexes of general formula $Fe(CNS)_x^{(3-x)+}$, where x is an integer from 1 to 6, and an attempt will be made to determine the stability constant of each. The stability constant is the reciprocal of the ionisation constant, *i.e.*,

$$K_x = [Fe(CNS)_x^{(3-x)+}]/[Fe(CNS)_{x-1}^{(4-x)+}][CNS^-] \quad . \quad . \quad . \quad . \quad . \quad (1)$$

and will be zero if the complex has no real existence.

The relationships expressed in equation (1) can be combined and rearranged so that the neutral complex appears in the denominator of each equation, thus,

$$[Fe(CNS)_x^{(3-x)+}][CNS^-]^{3-x}/[Fe(CNS)_3] = k_x \quad . \quad . \quad . \quad . \quad . \quad (2)$$

The simple ferric ion ($x = 0$) may conveniently be included in this series.

It is important to observe from this equation that the relative proportions of the different complexes, though dependent on the thiocyanate concentration, are quite independent of the iron concentration so long as this is not sufficiently great as to reduce appreciably the thiocyanate concentration by complex formation. Hence the importance in the colorimetric determination of ferric iron by thiocyanate of keeping the thiocyanate concentration constant.

* Part I, *J.*, 1951, 1310.

The effect is well seen in Figs. 1 and 2, which show families of curves, (1) at constant ferric concentration and (2) at constant thiocyanate concentration. In Fig. 1 the variation of the wave-length of maximum absorption indicates a change in the proportions of the various complexes.

If an aqueous solution is extracted with ether, then by the partition law,

$$[\mathrm{Fe(CNS)_n}]_{\mathrm{Water}} = n[\mathrm{Fe(CNS)_n}]_{\mathrm{Ether}} = n(\mathrm{Fe})_{\mathrm{E}} \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

whence, from (2),

$$[\mathrm{Fe(CNS)}_n^{3-n+}][\mathrm{CNS^-}]^{3-x}/(\mathrm{Fe})_{\mathrm{E}} = nk_n \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

If, under given conditions, nearly all the iron in the water were in the form of a single complex,

$$(\mathrm{Fe})_{\mathrm{W}} = [\mathrm{Fe(CNS)}_n^{3-n+}] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

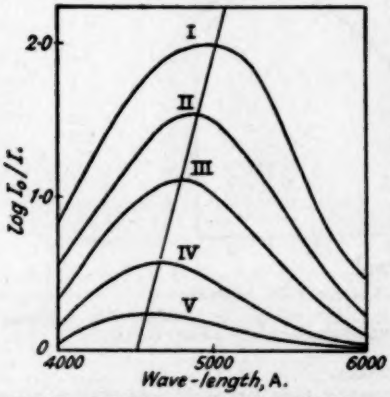
then, from (4)

$$[\mathrm{CNS^-}]^{3-x} = nk_n(\mathrm{Fe})_{\mathrm{E}}/(\mathrm{Fe})_{\mathrm{W}} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

The value of x can now be determined by plotting log $[\mathrm{CNS^-}]$ against log $(\mathrm{Fe})_{\mathrm{E}}/(\mathrm{Fe})_{\mathrm{W}}$; $[\mathrm{CNS^-}]$ is equal to the total thiocyanate concentration when this is in large excess. In other cases,

FIG. 1.

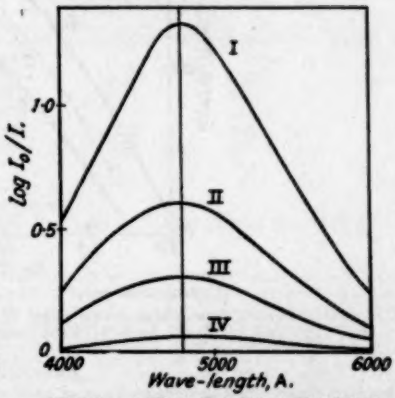
Absorption curves at varying thiocyanate concentration : $\lambda_{max.}$ varies.



$[\mathrm{Fe^{+++}}] = 0{\cdot}000303$M.; $[\mathrm{CNS^-}]$ = (I) 0·91M.; (II) 0·28M.; (III) 0·091M.; (IV) 0·028M.; (V) 0·009M.

FIG. 2.

Absorption curves at constant thiocyanate concentration : $\lambda_{max.}$ is constant, and Beer's law is obeyed.



$[\mathrm{CNS^-}] = 0{\cdot}37$M.; $\mathrm{Fe^{[+++]}}$ = (I) 0·00024M.; (II) 0·00012M.; (III) 0·00006M.; (IV) 0·000012M.

a correction for the thiocyanate combined in the complex must be made, after an approximate value for x has been found. The method becomes impracticable when the iron is in excess, and also when several complexes are simultaneously present in significant proportions.

Fig. 3 shows plots of log $[\mathrm{CNS^-}]$ against log $(\mathrm{Fe})_{\mathrm{E}}/(\mathrm{Fe})_{\mathrm{W}}$ for two experiments, and it will be seen that the slope in fact varies, over the range covered, from about $+2$ (= $\mathrm{FeCNS^{2+}}$) to -1 (= $\mathrm{Fe(CNS)_4^-}$), the curve passing through a maximum where the mean charge on the complex is zero. As it is evident that several complexes are present together, a more general solution of equation (4) must be found.

Since the total iron in the aqueous layer is the sum of the iron in the different complexes present, we may write, using equation (2),

$$(\mathrm{Fe})_{\mathrm{W}} = \sum_{x=6}^{x=0}[\mathrm{Fe(CNS)}_n^{3-n+}] = [\mathrm{Fe(CNS)_n}]\sum_{x=6}^{x=0}k_n[\mathrm{CNS^-}]^{(x-3)} \quad . \quad . \quad . \quad (7)$$

and hence, from (3),

$$(\mathrm{Fe})_{\mathrm{W}}/(\mathrm{Fe})_{\mathrm{E}} = nk_0[\mathrm{CNS^-}]^{-3} + nk_1[\mathrm{CNS^-}]^{-2} + \ldots\ldots + nk_6[\mathrm{CNS^-}]^3 \quad . \quad . \quad (8)$$

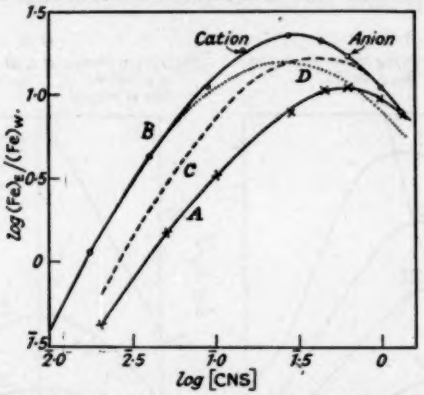
By making a sufficient number of accurate measurements of the partition ratio $(Fe)_W/(Fe)_E$ at different thiocyanate concentrations it is possible, in theory, to determine all the values of nk_n, and hence of the stability constants K_n which are connected with them by the relationship $K_n = k_n/k_{n-1}$.

The number of parameters in equation (8) is too large for practical purposes, but may be reduced as follows. First, it will be seen from equation (2) that $k_3 = 1$. Secondly, Frank and Ostwalt (*J. Amer. Chem. Soc.*, 1947, **69**, 1321) have shown that the value of K_1 $(= k_1/k_0)$ can be found from measurements of the optical density of solutions of low thiocyanate concentration. Thirdly, an empirical relationship has been found (see p. 1578) relating k_0 to k_4, k_1 to k_5, and k_2 to k_6. Thus the total number of unknowns to be found from the experiment may be reduced to the manageable number of three.

Equation (8) has been derived above without any reference to activity coefficients. A rigorous treatment, however, shows that the activity-coefficient factors all cancel out, and that precisely the same equation results, provided that these activity coefficients remain constant at constant ionic strength.

FIG. 3.

Logarithmic plot of extraction ratio against thiocyanate concentration.



Experimental points: × = *Series A*, ⊙ = *Series B.*

A, B, curves calculated from constants in Table III, cols. 2 and 3; D, calculated from constants in Table III, col. 4; C, curve A, partly corrected for variation in activity coefficients.

EXPERIMENTAL.

Partition experiments were carried out at 18·0° ± 0·1° at a constant acidity of 0·18N. and an ionic strength of 1·8. The choice of acid and salt used in making up the solutions was limited, as many anions form complexes with ferric iron. It is generally believed that neither nitrate nor perchlorate forms such complexes in dilute solution, and Rabinowitch and Stockmayer (*J. Amer. Chem. Soc.*, 1942, **64**, 335) found no evidence of complex formation up to concentrations of 3M. Two series of solutions were therefore made: series A with ferric nitrate, potassium thiocyanate, potassium nitrate, and nitric acid; series B with ferric perchlorate, ammonium thiocyanate, sodium perchlorate, and perchloric acid. According to Bray and Hershey's data (*ibid.*, 1934, **56**, 1889), an acidity of 0·18N. should reduce hydrolysis to about 1% of the simple ferric ion present, at the ionic strengths used in these experiments.

The solutions, especially those containing nitric acid, were rather unstable and the experiments were carried out as quickly as possible and to a strict timetable. Equilibrium is rapidly established, and the solutions were always shaken for 15 minutes, allowed to settle for 15 minutes, separated, and analysed at once. Basically, 200 ml. of 2M-thiocyanate were mixed with 50 ml. of 0·03M-ferric salt which had been made 0·9N. with respect to acid, and the whole extracted with 150 ml. of ether. In other runs of the series, varying amounts of the thiocyanate were replaced by equal amounts of 2M-salt. (In series B, the fall in ionic strength caused by the extraction of ferric thiocyanate and thiocyanic acid by the ether was calculated from preliminary experiments, and extra salt was added to maintain it at the value 1·8. This correction was not made in series A, where μ may have fallen to 1·65 in some cases.) The ether (AnalaR quality) was shaken with ferrous sulphate, washed, stored over copper wire to remove peroxides which interfere the determination of ferric iron, and distilled. The iron was determined by titanous sulphate, and the thiocyanate by silver nitrate. The total iron and total thiocyanate in the two layers were always checked against the amount originally taken, allowance being made for the change of volume of the ether and water layers caused by their mutual solubility. Agreement to within about 2% was obtained. The results are summarised in Fig. 3.

Optical density measurements were made in order to determine the value of K_1, at an ionic strength of 1·8 in the presence of several different salts, and also at ionic strengths of 1 and 0·2. The solutions used here consisted of 20 ml. of the base salt (sodium perchlorate, potassium nitrate, or lithium nitrate) to which were added 1 ml. of 0·005M-ammonium thiocyanate and 1—4 ml. of 0·05M-ferric salt, both acidified to 0·9N. with the appropriate acid, and the whole was made up to 25 ml. with 0·9N-acid. Small volumes were measured with a micrometer syringe. The resulting solutions were stable for several hours and were measured at room temperature in a Unicam spectrophotometer, concordant values of K_1 being obtained over the visible range from 3900 to 5500 A. The equation given by Frank and Ostwalt (*loc. cit.*) is: $ab/D = (a + b)/\varepsilon + 1/\varepsilon K_1$ where a = total ferric iron, b = total thiocyanate, D = optical density, and ε = molecular extinction coefficient. In a few cases, runs were made at several values of a, and both ε and K_1 were obtained graphically over the range of wave-lengths; but for the most part, pairs of runs were made with $a = 0{\cdot}002$ and 0·008, and the resulting simultaneous equations were solved. ε, depending as it does on the difference of two values of ab/D, is rather sensitive to experimental error, but as it is independent of the ionic strength or the nature of the base salt used, it was possible to take mean values from all the 26 experiments made at each wave-length, and these mean values, which are given in Table I, were used to determine K_1 in each separate run. The values of K_1 for all wave-lengths and every run of a particular salt solution were then collected and averaged, the results being given in Table II.

TABLE I.

Molecular extinction coefficients of $FeCNS^{2+}$, $(\log I_0/I)/lc$; *standard error* ±40.

λ	3800	3900	4000	4100	4200	4300	4400	4500	4600	4700	4800	4900	5000	5500	6000
ε	1617	1954	2646	3189	3793	4321	4693	4983	4946	4781	4474	4065	3578	1367	437·1

TABLE II.

Value of K_1 *in different salt solutions and ionic strengths.*

Salt.	μ.	K_1.	Activity coefficients. Pure salt.*[1]	$AgOAc$.[2]	$CH_2Cl{\cdot}CO_2Ag$.[2]	$CaSO_4$.[3]
$NaClO_4$	1·8	122·5 ± 1·0	(0·54)	—	—	0·6
KNO_3	1·8	91·0 ± 0·9	0·34	0·60	0·48	0·3
$LiNO_3$	1·8	114·4 ± 5	(0·85)	0·47	0·49	0·4
$NaClO_4$	1·0	127·9 ± 6	0·576	—	—	—
KNO_3	1·0	98·8 ± 4	0·439	0·75	0·53	—
$LiNO_3$	1·0	109·5 ± 5	0·54	0·55	—	—
$HClO_4$	0·2	178·2 ± 7	—	—	—	—
HNO_3	0·2	196·4 ± 8	—	—	—	—

* Values in parentheses were obtained by extrapolation.
[1] Landolt–Börnstein "Tabellen." [2] MacDougall and Rehner, *J. Amer. Chem. Soc.*, 1934, **56**, 368.
[3] This work (approximate value only).

A few migration experiments were performed to confirm the conclusions reached as to the mean charge on the complexes at different thiocyanate concentrations. To be of value, conditions must be arranged so that the thiocyanate concentration on each side of the moving boundary is nearly the same, so that the equilibrium between the different complexes is not disturbed as the boundary is crossed. The apparatus used was a U-tube with a wide-bore stop-cock in each limb. The portion between the stop-cocks was filled with acidified thiocyanate, coloured by the addition of a trace of ferric iron. The remaining portions were filled with the same acidified solution of thiocyanate but without the iron. After the whole had been brought to uniform temperature in a thermostat, the boundaries were formed by opening the stop-cocks. These boundaries were apt to become unstable, but by use of a low potential gradient definite results were obtained. Only small movements were obtained, however, as on prolonged running secondary effects intervened, such as the migration of hydroxyl ions from the cathode, with consequent hydrolysis and bleaching of the boundary.

DISCUSSION.

It will be seen from Fig. 3 that the slope of the graph of $\log (Fe)_R/(Fe)_W$ against $\log [CNS^-]$ changes direction, showing that positive complexes predominate at low thiocyanate concentrations and negative complexes at high concentrations (equation 6). This was confirmed by migration experiments. With a concentration of thiocyanate of 0·09287N., the boundary moved towards the cathode: at 0·6339N., it moved to the anode (both solutions being made up to $\mu = 1{\cdot}8$ with sodium perchlorate). The two points are marked "cation" and "anion" in Fig. 3.

Fig. 3 indicates that the series in potassium nitrate (*A*) and that in sodium perchlorate (*B*) are generally similar though they do not follow exactly the same course, and that curve B, at least, shows a remarkable symmetry. This symmetry, which is assumed to apply also to curve *A*, means that if the equation is transformed to bring the origin to the point of maximum extraction, positive and negative logarithmic terms become interchangeable, and therefore that in equation (8), the coefficients of like powers (but opposite signs) of $[CNS^-]$ become equal. The

origin is shifted by multiplying $[CNS^-]$ by a factor P (the maximum in Fig. 3 lies at $-\log P$), and equation (8) can then be written as

$$(Fe)_W/(Fe)_B = \frac{nk_0}{P^{-3}}P^{-3}[CNS^-]^{-3} + \frac{nk_1}{P^{-2}}P^{-2}[CNS^-]^{-2} + \ldots + \frac{nk_6}{P^3}P^3[CNS^-]^3$$

$$= k_0'P^{-3}[CNS^-]^{-3} + k_1'P^{-2}[CNS^-]^{-2} + \ldots + k_6'P^3[CNS^-]^3 \qquad (9)$$

in which $k_0' = k_6'$, $k_1' = k_5'$, and $k_2' = k_4'$. Remembering that $k_1/k_0 = K_1$, we may write

$$(Fe)_W/(Fe)_B = uk_0' + vk_2' + k_3' \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (10)$$

where $u = (P^3[CNS^-]^3 + P^{-3}[CNS^-]^{-3} + K_1P^{-3}[CNS^-]^{-2} + K_1P[CNS^-]^3)$

and $v = (P^{-1}[CNS^-]^{-1} + P[CNS^-])$. Equation (10) was solved by the method of least squares for the eight experimental points of series A and the nine experimental points of series B, and the results are given in Table III.

TABLE III.

	Series A.	Series B.	Series B, calc. by Bjerrum's theory.
P	1·68	3·365 ± 0·005	—
a	(1·39 ± 0·144) × 10^{-5}	(3·352 ± 0·16) × 10^{-5}	—
b	(4·69 ± 0·59) × 10^{-2}	(2·054 ± 0·10) × 10^{-2}	—
c	(− 4·03 ± 15·1) × 10^{-3}	(− 1·008 ± 2·07) × 10^{-3}	—
nk_0	2·93 × 10^{-6}	0·879 × 10^{-6}	1·045 × 10^{-6}
nk_1	2·665 × 10^{-4}	1·077 × 10^{-4}	1·28 × 10^{-4}
nk_2	2·79 × 10^{-2}	6·09 × 10^{-3}	3·92 × 10^{-2}
nk_3	< 11·1 × 10^{-3}	< 1 × 10^{-2}	3·005 × 10^{-2}
nk_4	7·87 × 10^{-2}	6·90 × 10^{-3}	5·76 × 10^{-4}
nk_5	2·12 × 10^{-3}	1·38 × 10^{-3}	2·77 × 10^{-3}
nk_6	6·59 × 10^{-4}	1·28 × 10^{-3}	3·34 × 10^{-6}
K_1	91 ± 0·9	122·5 ± 1·0	(122·5)
K_2	105·4 ± 17	56·5 ± 3·7	30·65
K_3	< 0·39	< 0·184	7·67
K_4	> 0·717	> 62·8	1·92
K_5	0·027 ± 0·004	0·200 ± 0·013	0·481
K_6	0·031 ± 0·005	0·0926 ± 0·006	0·1205

It is unfortunate that in each case the value of nk_3 is less than its experimental error. It must be positive, since $k_3 = 1$ and n is the partition coefficient, and the best that can be done is to indicate a "maximum" value, obtained by adding the standard error to the observed figure.

We must now consider why the two series do not give identical results. There are two possible reasons. The first is that in spite of Rabinowitch and Stockmayer's evidence (*loc. cit.*), a complex may be formed between the ferric and the nitrate ions. The second is that the activity coefficients of the reacting substances may change even at constant ionic strength when one salt is substituted for another. The activity coefficients of ammonium thiocyanate and of sodium perchorate at high concentration do not appear to be accurately known, but both are probably about 0·54 at 1·8M. It is reasonable to assume that the activity of a small amount of a third substance dissolved in a mixture of these two will not be greatly affected by the proportions of the two salts in the mixture. This is borne out by the symmetry in Curve B, which could scarcely survive any marked change in activity coefficient.

In contrast with the above, the activity coefficient of potassium thiocyanate and potassium nitrate are respectively 0·56 and 0·34 at 1·8M., and it is probable that the activity of a third substance will be considerably affected by the proportions of the two salts, so that a rather large systematic error will be introduced. We cannot be certain that even series B is quite free from this error, but it is clearly much more reliable than series A.

In order to obtain more evidence on the magnitude of the effects likely to result from changing from one salt to another, some measurements were made of the value of K_1 by the optical method, lithium nitrate being used instead of potassium nitrate. The results of these experiments, and also some at lower salt concentrations, are given in Table II. It can be seen that the variations in K_1 are of the same order as the variations in the activity coefficients of various salts as determined by their solubilities. There is no evidence of specific interaction with the nitrate ion.

The various complexes, being differently charged, will have different activity coefficients, and without a knowledge of these individual values, it is not possible to predict accurately

what the effect on the extraction ratio will be of changing these by altering the base salt. An approximate calculation can be made if we assume that each of the activity coefficients, except that of the neutral complex, which will remain unity, is changed in the same ratio, f_R, when the change of salt is made. f_R for the complexes in 1·8M-potassium nitrate solution (as compared with 1·8M-ammonium thiocyanate) is given by the ratio of K_1 in the two salts (=91·0/122·5 = 0·742), and the values for mixtures of these two salts can be found by assuming that log f_R varies linearly with the concentration of nitrate in the mixture. It is then found that

$$k_0^A = k_0^B/f_R^4;\ k_1^A = k_1^B/f_R^3;\ k_2^A = k_2^B/f_R^2;\ k_3^A = k_3^B;$$
$$k_4^A = k_4^B;\ k_5^A = k_5^B f_R \text{ and } k_6^A = k_6^B \cdot f_R^2$$

[where k_x^A and k_x^B are the constants of equation (8) in series A and series B, respectively], so it is possible from equation (8) to calculate $(Fe)_W/(Fe)_E$ for solutions of series A by using the constants found experimentally from series B. The resulting graph (Curve *C*, Fig. 3) shows that this approximate calculation partly accounts for the difference between the two series. We cannot tell whether a correction based on accurately known activity coefficients would bring about exact coincidence or not, but it is significant that the greatest relative divergence between Curves *A* and *C* lies in the region where we know least about the activity coefficients, that is, where negative complexes are present in large proportion.

Bjerrum (*Z. physikal. Chem.*, 1923, **106**, 219) suggested that in the case of symmetrical weak acids, the dissociation constants were connected by the relationship

$$K_1/K_2 = K_2/K_3 = \ldots = Q \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (11)$$

This relationship follows if we assume that the free energies of the different complexes differ from one another only in the electrostatic work required to remove the thiocyanate ion to infinity, a quantity which will increase in regular increments from one complex to the next. Though this is undoubtedly an over-simplification, Bjerrum's relationship seems to give reasonable results in a number of cases. The uncertainty in the value of k_3 (which affects both K_3 and K_4) makes a direct test of this hypothesis impossible with the figures obtained in this work, but the theory may be tested in another way. By combining equations (8) and (11), we find

$$(Fe)_W/(Fe)_E = k_0[CNS^-]^{-3} + k_0K_1[CNS^-]^{-2} + k_0K_1^2Q[CNS^-]^{-1} + k_0K_1^3Q^2$$
$$+ k_0K_1^4Q^3[CNS^-] + k_0K_1^5Q^{10}[CNS^-]^2 + k_0K_1^6Q^{15}[CNS^-]^3 \quad . \quad (12)$$

Q is most easily found by assuming the logarithmic curve to be symmetrical, and by equating, for example, the coefficient of $[CNS^-]^{-3}$ to that of $[CNS^-]^3$ after shifting the origin to that used in the solution of equation (9), thus: $k_0/P^{-3} = k_0K_1^6Q^{15}P^{-3}$, P and K_1 being known. Equation (12) is then solved for any one experimental point to obtain k_0, and the other constants follow. Since, however, there is a possibility that a systematic error has been caused by substituting ammonium thiocyanate for sodium perchlorate progressively throughout the series, and since K_1 is measured in excess of perchlorate, it is probably sounder not to assume that the point of symmetry is the same as that found experimentally, but to solve equation (12) for the two experimental points where the perchlorate concentration was highest. This may be done graphically. The results are given in Table III, column 4, and the values of log $(Fe)_E/(Fe)_W$ worked out from these are plotted in Fig. 3, Curve *D*.

Curves *B* and *D* are in only approximate agreement, but they show a very marked similarity, and the agreement may possibly be within the limits of a systematic error caused by changing activity coefficients. This seems to show that the complexes differ in stability from one another mainly in the electrostatic strength of their bonds. There must be a considerable covalent contribution to the bond strength, since even the negative complexes are fairly stable; but either this contribution is about the same for all complexes, or it also varies in regular steps with the charge. There are other factors contributing to the stability, such as the symmetry of the complex, and also the heat of hydration caused by the orientation of the solvent dipoles round the charged ions, which cannot be expected to vary in equal steps through the series. The accuracy of the experiments is not sufficient to enable us to gauge even approximately the importance of these factors, except to say that they are evidently not predominating.

The ferric ion forms complexes with many other anions, and its seems probable that the partition method could be used to determine the stability constants in many cases where one of the complexes is a neutral molecule. It is noteworthy that the ability of ethers to extract ferric chloride (Dodson, Forney, and Swift, *J. Amer. Chem. Soc.*, 1936, **58**, 2573; Nachtrieb and Conway, *ibid.*, 1948, **70**, 3547) passes through a maximum similar to the maximum found in the

present work, at a chloride concentration of about 6—10M. This seems to indicate that negative complexes of the type $FeCl_4^-$ to $FeCl_6^{3-}$ predominate at these concentrations, and migration experiments in 11M-acid, carried out in the apparatus described above, though not very definite, seemed to bear out this conclusion. (In their spectroscopic study, Rabinowitch and Stockmayer detected the presence of the lower complexes $FeCl^{2+}$ to $FeCl_3$, and found some evidence of negative complexes at chloride-ion concentrations of about 10M.)

UNITED COLLEGE, ST. ANDREWS. [*Received, November 13th*, 1950.]

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357. *Heterogeneous Catalysis of the Racemisation of (+)-1-Phenylethyl Bromide.*

By C. L. ARCUS and G. V. BOYD.

(+)-1-Phenylethyl bromide in solution in carbon tetrachloride saturated with hydrogen bromide at 73° undergoes racemisation only at a solid surface; the mechanism of racemisation is discussed. Under the conditions employed, the order of effectiveness in catalysis of racemisation is: silver bromide > charcoal > powdered glass ≫ potassium bromide. The presence of styrene dibromide in the solution accelerates racemisation.

(+)-1-Phenylethyl bromide with bromine in carbon tetrachloride becomes racemised, but some substitution to form hydrogen bromide and (optically inactive) styrene dibromide occurs, and it is uncertain whether bromine-exchange between 1-phenylethyl bromide and elementary bromine takes place; when silver bromide is present racemisation is rapid.

IT was observed (Arcus, Campbell, and Kenyon, *J.*, 1949, 1510) that 1-phenylethyl bromide in solution in carbon tetrachloride racemised rapidly when heated under reflux in the presence of silver bromide and bromine. Hydrogen bromide was evolved during the heating and a small quantity of a compound, shown below to be styrene dibromide, was isolated. Racemisation was much less rapid with bromine alone, and slight with silver bromide alone. The formation of styrene dibromide on heating 1-phenylethyl bromide with bromine was observed by Schramm (*Ber.*, 1885, **18**, 354). In the present investigation, the rates of racemisation of 1-phenylethyl bromide in solution in carbon tetrachloride containing hydrogen bromide or bromine in the presence of various solids, have been measured.

The rate of racemisation of 1-phenylethyl bromide in solution in anhydrous acetone in the presence of dissolved lithium bromide was found to be twice the rate of halogen-exchange as determined by the use of lithium bromide containing radioactive bromine (Hughes, Juliusberger, Scott, Topley, and Weiss, *J.*, 1936, 1173), whence the racemisation is due to bimolecular halogen-exchange:

$$Br^- + PhMeHC{-}Br \xrightarrow{S_N2} Br{-}CHMePh + Br^-$$

occurring in homogeneous solution. 1-Phenylethyl chloride has been observed to undergo homogeneous unimolecular racemisation in solution in sulphur dioxide (Bergmann, Polanyi, and Szabo, *Z. physikal. Chem.*, 1933, *B*, **20**, 161):

$$CHMePhCl \rightleftharpoons CHMePh^+ + Cl^-$$

racemisation being due to dissociation to give the planar carbonium ion. Racemisation of 1-phenylethyl chloride occurs by an allied mechanism in the presence of heavy-metal chlorides in solution in organic solvents (Böhme and Bodendorf, *Annalen*, 1935, **516**, 1; Böhme, *Ber.*, 1938, **71**, 2372); a complex is formed which ionises:

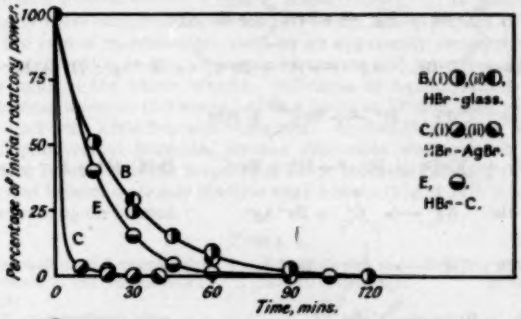
$$CHMePhCl + MCl_n \rightleftharpoons CHMePh[MCl_{n+1}] \rightleftharpoons \overset{+}{C}HMePh + [MCl_{n+1}]^-$$

This mechanism receives support from the facts that an increase in the dielectric constant of the solvent generally increased the rate of racemisation, and that addition of hydrogen chloride or lithium chloride diminished the rate of racemisation by competing with the organic halide for complex-formation with the heavy-metal chloride. Both unimolecular and bimolecular homogeneous racemisations in the presence of constant concentrations of added reagents give rise to a first-order fall in optical rotation, and, as indicated above, other data are necessary to distinguish these two mechanisms.

1-Phenylethyl bromide underwent 10% racemisation in 5 hours when kept at 73° in solution

in carbon tetrachloride saturated with hydrogen bromide (Fig. 2, *A*). A saturated solution of hydrogen bromide in carbon tetrachloride had no measurable conductivity, and hence hydrogen bromide does not dissociate in this solvent. It is inferred that the racemisation in *A* did not arise by any mechanism (*e.g.*, bimolecular substitution similar to that with lithium bromide in acetone) which requires appreciable concentrations of ions in homogeneous solution; the rate of racemisation in the presence of hydrogen bromide increased on increasing the surface by the addition of powdered glass (Fig. 1, *B*) and it is concluded that the racemisation in *A* occurred at the glass surface of the flask. A 38-fold increase in surface resulted in a 130-fold increase in the initial velocity of racemisation (Table I). The fractured glass surfaces thus appear more efficient than the fused surface of the flask; a similar effect for the exchange of bromine between hydrogen bromide and ethyl bromide at 180—260° was observed by Peri and Daniels (*J. Amer. Chem. Soc.*, 1950, **72**, 424).

FIG. 1.



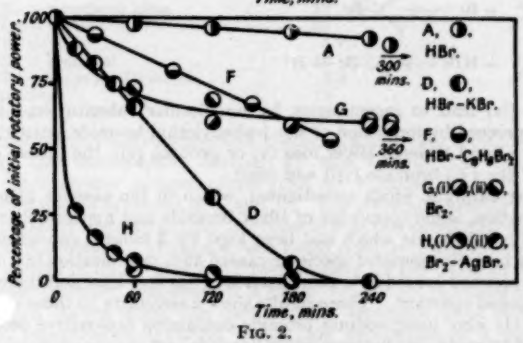
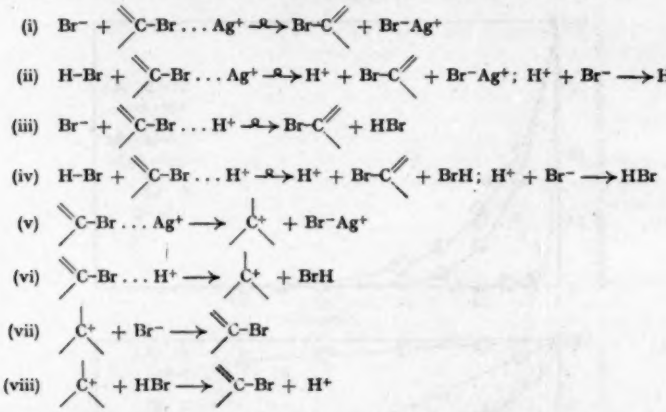


FIG. 2.

Racemisation was most rapid with hydrogen bromide in the presence of silver bromide; the initial rate was 320 times that for *A*, and the solution was optically inactive after 30 minutes (Fig. 1, *C*). Senter (*J.*, 1910, **97**, 346) observed that the silver bromide formed has a marked catalytic effect on the hydrolysis of α-bromopropionic and α-bromo-*n*-butyric acids in aqueous silver nitrate; a similar effect was noticed by Baker (*J.*, 1934, 987) for the alcoholysis of benzyl bromide by ethyl-alcoholic silver nitrate. Kappanna (*Proc. Indian Acad. Sci.*, 1935, **2**, *A*, 512) concluded that in the reaction of sodium α-bromopropionate with aqueous silver nitrate, reaction occurs almost entirely between α-bromopropionate ions and silver ions adsorbed on the surface of the silver bromide. Cowdrey, Hughes, Ingold, and Masterman (*J.*, 1937, 1236, 1243) concluded from the stereochemical and kinetic evidence that the following reactions, *viz.*, (i) hydrolysis and alcoholysis of 2-*n*-octyl bromide in aqueous alcohol containing suspended silver oxide or dissolved silver nitrate or acetate, (ii) hydrolysis of 1-phenylethyl chloride in aqueous acetone with suspended silver oxide, (iii) methoxylation of methyl α-bromopropionate with methyl-alcoholic silver nitrate, and (iv) the hydrolysis of the acid and its sodium salt with a suspension of silver oxide in water or aqueous acetone, proceed wholly or partly by reaction

between the halogen-containing organic molecule (or the anion in the cases of the acid and its salt) adsorbed on to the silver halide surface, and that of the silver oxide when present, and the hydroxylic solvent or a hydroxyl or alkoxyl ion. The carbon–halogen bond of the adsorbed halide is stretched and weakened, an adsorbed silver ion detaches the halogen, and the resulting carbonium cation reacts with an adsorbed solvent molecule or appropriate reagent ion. (+)-1-Phenylethyl chloride in benzene solution yielded with silver nitrite a largely racemised 1-phenylethyl nitrite (Eastman and Ross, *J. Amer. Chem. Soc.*, **1946**, **68**, 2398) in accord with reaction *via* dissociation of the organic halide on the silver nitrite–silver chloride surface.

It is considered that the silver bromide in the present experiments functioned similarly. The alkyl–bromine bond of an adsorbed 1-phenylethyl bromide molecule is weakened by the interaction of silver ions with the bromine. The adsorbed hydrogen bromide functions as reagent, either by supplying bromide ions (i) or directly (ii). Further, the functions of the silver ions may be in part taken over by adsorbed protons, as in (iii) and (iv):


(i) Br⁻ + C–Br ... Ag⁺ → Br–C + Br⁻Ag⁺
(ii) H–Br + C–Br ... Ag⁺ → H⁺ + Br–C + Br⁻Ag⁺; H⁺ + Br⁻ → HBr
(iii) Br⁻ + C–Br ... H⁺ → Br–C + HBr
(iv) H–Br + C–Br ... H⁺ → H⁺ + Br–C + BrH; H⁺ + Br⁻ → HBr
(v) C–Br ... Ag⁺ → C⁺ + Br⁻Ag⁺
(vi) C–Br ... H⁺ → C⁺ + BrH
(vii) C⁺ + Br⁻ → C–Br
(viii) C⁺ + HBr → C–Br + H⁺

The reactions (i)—(iv) lead to racemisation by bimolecular substitution. Some part of the racemisation may proceed by ionisation of the 1-phenylethyl bromide assisted by weakening of the carbon–bromine bond through silver ions (v) or protons (vi), the planar carbonium cation combining to yield the (±)-bromide (vii) and (viii).

Unlike the other catalytic solids investigated, which in the absence of hydrogen bromide effected no racemisation, some specimens of silver bromide had appreciable racemising effect: (*a*) a specimen of silver bromide which had been kept for 3 months caused no racemisation in 2 hours at 73°; (*b*) a recently-prepared specimen caused 39% racemisation in 2 hours; (*c*) another recently-prepared specimen caused 22% racemisation in the first hour and thereafter the rotation of the solution remained constant. These results show a similarity to those of Langer (*J. Chem. Physics*, **1943**, **11**, 11) who, using sodium bromide containing radioactive bromine, found that there is exchange of bromide ions between silver bromide and aqueous sodium bromide at a rate which decreases with the age of the silver bromide, and finally ceases. Racemisation in the presence of silver bromide alone must proceed by (i) or by (v) followed by (vii), the bromide ion here being that normally present in the silver bromide lattice only.

The much greater rate of racemisation with hydrogen bromide–silver bromide than with silver bromide alone points to attack by adsorbed hydrogen bromide (ii) or bromide ions derived therefrom (i), *i.e.*, to racemisation through inversion mechanisms. Nevertheless, the possibility that some part of the effect of the hydrogen bromide lies in providing adsorbed protons which assist the ionisation of 1-phenylethyl bromide (vi), as well as promoting inversion by mechanisms (iii) and (iv), is not excluded.

The system hydrogen bromide–potassium bromide is much less effective in racemisation than hydrogen bromide–silver bromide, probably owing to the lesser capacity for adsorption of the potassium bromide surface (Fig. 2, *D*).

In the presence of hydrogen bromide–charcoal, the initial rate of racemisation of 1-phenylethyl bromide was slightly less than half that in the presence of hydrogen bromide–silver bromide (Fig. 1, *E*).

Since glass, potassium bromide, and charcoal do not themselves effect racemisation, it is concluded that racemisation when hydrogen bromide is present is due to the operation on the solid surfaces of inversion mechanisms (iii) and (iv) together, possibly, with the ionisation mechanism (vi) followed by (vii) and (viii).

When hydrogen bromide was passed through a solution of 1-phenylethyl bromide in carbon tetrachloride containing styrene dibromide (Fig. 2, *F*), the rate of racemisation was 7 times that for *A*. The mechanism whereby the rate is increased is not known.

The racemisation of any compound by any mechanism in which enantiomeric molecules of the compound suffer reaction at the same rate would be expected to occasion a first-order fall in rotation, provided that conditions are kept constant. In the present work (which was designed to give comparative rates only), racemisation in *B* and *E* was of first-order [for *B* (i), *B* (ii), and *E*, k is 0·045, 0·043, and 0·068 min.$^{-1}$, respectively); *A* and *C* were respectively too slow and too fast to permit an estimation of the order; and racemisation in *D* and *F* was zero order (for *D* and *F*, k is 0·0026 and 0·00095 mole l.$^{-1}$ min.$^{-1}$, respectively)]. It is possible that during the last two experiments there occurred the formation of an active surface or complex at a rate comparable with the rate of racemisation, yielding an apparently zero-order racemisation.

The course of racemisation in the presence of bromine and bromine–silver bromide is now considered in the light of the above results. Solutions of 1-phenylethyl bromide in carbon tetrachloride containing bromine (1·0 equiv.) after 4 hours at 73° lost 40% of the initial rotatory power (Fig. 2, *G*) and very little bromine remained. Hydrogen bromide was evolved and, in addition to (±)-1-phenylethyl bromide, styrene dibromide was isolated at the end of the experiment. Similar solutions in the presence of silver bromide lost 94% of the initial rotatory power in one hour and became optically inactive after 3 hours (Fig. 2, *H*); hydrogen bromide and styrene dibromide were again formed.

TABLE I.

Expt.	Racemisation of 1-phenylethyl bromide in the presence of:	Racemisation in first 10 mins., %.	Relative extent of racemisation in first 10 mins.
A	HBr	0·3	1
B	HBr + powdered glass	38	130
C	HBr + AgBr	97	320
D	HBr + KBr	5·7	19
E	HBr + charcoal	43	140
F	HBr + styrene dibromide	2·2	7
G	Bromine	10	33
H	Bromine + AgBr	66	220

Thus in the experiments involving bromine, the system hydrogen bromide–styrene dibromide was present, but the racemisation effected by this system, the components of which were present in much smaller concentrations than for *F*, could not have been more than a fraction of the racemisation observed in *G* and *H*. The styrene dibromide isolated from these experiments was optically inactive so that, in proportion as this compound was formed, optically active material was diminished. It has not been found possible to deduce from the data whether or not these two sources of loss of rotatory power account for the whole of the loss occurring in the absence of silver bromide. Assessment is made difficult by the racemisation of 1-phenylethyl bromide which occurs when this compound is separated from styrene dibromide by distillation; 39% racemisation occurred during the distillation of a prepared mixture at 88°/19 mm. Gerrard (*J.*, 1945, 852) found certain specimens of 1-phenylethyl bromide to undergo extensive racemisation on redistillation. It is thus uncertain whether 1-phenylethyl bromide undergoes exchange of bromine ions or atoms with elementary bromine, except that the rate of exchange under the conditions employed cannot be rapid.

In the bromine–silver bromide experiments there was present, in addition to the two sources of loss of rotatory power described above, the system hydrogen bromide–silver bromide which has been shown to be very effective in racemisation; the possible catalytic effect of silver bromide on bromine-exchange between 1-phenylethyl bromide and elementary bromine could not be detected in the presence of these other sources of loss of optical activity. An equation of kinetic order 1·8 empirically satisfies the fall in rotatory power [k for *H* (i) is 0·28 mole$^{-0.8}$ l.$^{0.8}$ min.$^{-1}$] but, since the concentrations of bromine and hydrogen bromide alter with time, the value 1·8 has no simple significance.

EXPERIMENTAL.

(±)-1-Phenylethyl alcohol was resolved by Downer and Kenyon's method (*J.*, 1939, 1156). The optically active bromide was prepared by an unpublished method due to Dr. W. Gerrard: phosphorus oxybromide (17·2 g., 0·66 mol., prepared according to Gerrard, Nechvatal, and Wyvill, *Chem. and Ind.*,

1947, **29**, 437) in carbon disulphide (20 ml.) was added dropwise to a solution of (−)-1-phenylethyl alcohol (α_D^{17} −44·35°, *l* 1·0; 11 g.) and pyridine (14·4 g., 2 mols.) in carbon disulphide (40 ml.) at −10°. After 2 hours the reaction mixture was filtered, and the filtrate washed with dilute sulphuric acid, aqueous sodium carbonate, and water, and dried (K_2CO_3). After removal of the carbon disulphide under reduced pressure the residue was distilled and gave (+)-1-phenylethyl bromide (7·0 g., 42%), b. p. 86—87°/11 mm., n_D^{21} 1·5605, α_D^{22} +130·96° (*l* 1·0).

(±)-1-Phenylethyl bromide was prepared from the (±)-alcohol and hydrobromic acid (*d* 1·49) by the method of Norriss, Watt, and Thomas (*J. Amer. Chem. Soc.*, 1916, **38**, 1078); it was twice redistilled and had b. p. 84—84·5°/10 mm., and the variation of n_D with temperature was determined:

t	17°	18°	19°	20°	21°	22°	23°	24°	25°
n_D	1·5634	1·5629	1·5625	1·5619	1·5614	1·5609	1·5604	1·5599	1·5595

Carbon tetrachloride was kept over calcium chloride, distilled from fresh reagent, and the process repeated with phosphoric oxide; it was kept over the latter and distilled immediately before use.

Silver bromide was prepared by adding a slight excess of aqueous potassium bromide (10%) to aqueous silver nitrate (10%); it was washed by thrice boiling with water and filtering, dried at 100°, powdered, and again dried at 100°. Potassium bromide was dried by heating at 150°/20 mm. for 2 hours. Absorbent charcoal (B.D.H.; coarse grains) was dried by heating at 150°/1 mm. for 2 hours. Silica (B.D.H.) was powdered and dried by heating at 150°/2 mm. for 2 hours.

Pyrex glass tubing was washed with concentrated nitric acid and water, dried at 150°, powdered, and sieved mechanically; the portion which passed through a 1/100-inch mesh but not a 1/150-inch mesh was collected, boiled with aqua regia and then 4 times with water, and dried at 130° for 4 hours. The surface area of the glass powder was determined by Kendrick's method (*J. Amer. Chem. Soc.*, 1940, **62**, 2838) and that of Barrett, Birnie, and Cohen (*ibid.*, p. 2841) which depends on the fact that the average of the areas of projection of a unit plane in all random positions is $\frac{1}{4}$ unit, whence the average area of projection of a solid is $\frac{1}{4}$ of its surface area, since half the planes constituting the surface mask the other half. Small quantities of glass powder were placed on a microscope slide (*a*) by sprinkling, (*b*) by lowering the slide on to a small heap, whereupon, when the slide was withdrawn, a layer of powder adhered. Three slides were prepared by each method and photographed at linear magnification 75, and the areas of the images of the particles on the photographic plate measured with a planimeter. The number of particles per g. (*N*) was determined by weighing small quantities of powder on a microbalance and counting them on a ruled slide under a low-power microscope: found, (i) $1·039 \times 10^8$, (ii) $1·036 \times 10^8$. Then, where *A* = average area of a particle image, the surface area per g. of powder = $4AN/75^2$ = 710 cm.²/g.

Bromine was kept with phosphoric oxide for 3 days and then distilled from fresh reagent.

Hydrogen bromide was prepared by passing hydrogen saturated with bromine through a heated tube and then through a column packed with copper turnings (to remove any unreacted bromine) (*Org. Synth.*, Coll. Vol. II, p. 338). At the beginning and end of each experiment the rate of passage of hydrogen bromide was determined by passing the gas into water (50 ml.) for 5·0 minutes and titrating the solution with 0·1N-sodium hydroxide. The absence of bromine in the hydrogen bromide was confirmed by testing a similarly prepared solution with potassium iodide and starch.

TABLE II.

Expt.	1-Phenylethyl bromide, g.	CCl_4 to, ml.	Additional reagents.
A	2·00	20	HBr, 2·3 g./hr.
B (i)	1·00	10	,, 2·2 ,, ; glass, 1·00 g.
B (ii)	1·00	10	,, 2·1 ,, ; glass, 1·00 g.
C (i)	1·00	10	,, 2·3 ,, ; AgBr,* 2·00 g.
C (ii)	2·00	20	,, 2·2 ,, ; AgBr, 4·00 g.
D	1·50	15	,, 2·1 ,, ; KBr, 1·50 g.
E	1·70	17	,, 2·2 ,, ; charcoal, 0·57 g.
F	1·00	10	,, 2·5 ,, ; styrene dibromide, 0·50 g.
G (i)	3·85	40	Bromine,† 1 equiv.
G (ii)	2·00	20	,, 1 ,,
H (i)	2·00	20	,, 1 ,, ; AgBr, 4·00 g.
H (ii)	3·00	30	,, 1 ,, ; AgBr, 6·00 g.

* Freshly prepared. † Added as a standard solution in CCl_4.

Procedure.—The solution of 1-phenylethyl bromide in carbon tetrachloride and the additional reagents were placed in a 50-ml. Pyrex flask fitted (ground-glass joint) with a condenser through which, in those experiments in which hydrogen bromide was used, passed an inlet tube reaching nearly to the bottom of the flask, and to which was fitted an exit tube bearing a calcium chloride tube. The flask was immersed in a thermostat kept at 73·4° ± 0·1° and, in experiments in which a solid was present, the flask was shaken by attaching it to a motor-driven crank. Portions (1—2 ml.) of solution were withdrawn initially and at intervals, and the rotatory power determined; in the experiments with bromine, the withdrawn portion was washed with aqueous sodium sulphite (15%) and dried (Na_2SO_4) for 10 minutes before determination of the rotatory power. The reagents used are given in Table II.

In the experiments *A* and *F*, in which racemisation occurred slowly, correction was made for the concentration of the solution by evaporation of the solvent in the course of the experiment. The flask and the contents were weighed initially, before withdrawing each specimen for the determination of

rotation, and after returning the specimen to the flask. Then, where α_0, w_0 are the initial rotation and weight of the solution and α_t, w_t are the rotation after time t and the weight immediately before withdrawing the specimen for determination of this rotation, we have $\alpha_{\text{unracemised},\,t} = \alpha_0 w_t/w_0$, where $\alpha_{\text{unracemised},\,t}$ is the rotation the solution would have exhibited had evaporation only, without racemisation, occurred. The percentage of initial rotatory power after time $t = 100\alpha_t w_t/\alpha_0 w_0$. Further, where w'_t is the weight of solution after replacing the specimen used for rotation, and $\alpha_{t'}$, $w_{t'}$ are the rotation after t' and the weight immediately before the determination of rotation, we have $\alpha_{\text{unracemised},\,t'} = \alpha_0 w_0 w'_{t'}/w_t w_{t'}$, and the percentage of initial rotatory power after time $t' = 100\alpha_{t'} w_t w_{t'}/\alpha_0 w_0 w'_t$. In this way corrections were applied for both the concentration of the solution due to evaporation and the small manipulative losses ($w_t - w'_t$, etc.).

In a number of experiments the solution remaining at the end was washed with aqueous sodium carbonate, if hydrogen bromide was present, or with aqueous sodium sulphite, if bromine was present, and with water, and dried (Na_2SO_4). Carbon tetrachloride was removed under reduced pressure, and the residue distilled, yielding 1-phenylethyl bromide having the following characteristics :

Expt.	*A*.	*B* (i).	*C* (ii).	*D*.	*E*.	*G* (i).	*G* (ii).	*H* (ii).
n_D	1·5619	1·5623	1·5628	1·5622	1·5611	1·5654	1·5589	1·5648
t	20°	19°	18°	20°	22°	18°	25°	18°
% of original rotatory power	84	Nil	Nil	Nil	Nil	51	25	Nil

From *G* (i) was obtained a fraction, b. p. 125—132°/10 mm., which solidified; after repeated recrystallisation from ethyl alcohol it yielded styrene dibromide, m. p. 72—73°, optically inactive in ethyl alcohol. The residue from *G* (ii), after distillation of the 1-phenylethyl bromide, was optically inactive in solution in ethyl alcohol and similarly yielded styrene dibromide, m. p. 72·5—73·5° alone and mixed with a specimen of m. p. 73—73·5° prepared according to Glaser (*Annalen*, 1870, **154**, 154). The residue from *H* (ii) also yielded styrene dibromide, m. p. 72°. A larger quantity of the bromination product was prepared, in order to confirm its identity, as follows : bromine (4·9 g., 4·2 equivs.) was added dropwise to (±)-1-phenylethyl bromide (2·7 g.) containing a little iodine : hydrogen bromide was evolved. The mixture was heated for 3 hours on a steam-bath and kept overnight. The solid product was washed with 3N-sodium hydroxide and with water and dried; it (3 g.) was distilled, and the fraction, b. p. 148—151°/22 mm., was thrice recrystallised from light petroleum, giving needles, m. p. 70—72°, undepressed by the materials from *G* (i) and *H* (ii). Oxidation of this bromo-compound (5 g.) with potassium permanganate (10 g.) and sodium carbonate (2·5 g.) in water (240 ml.) gave benzoic acid (1 g.) which, twice recrystallised from water, had m. p. 120—121° alone and mixed with an authentic specimen.

Control Experiments.—A solution of (−)-1-phenylethyl bromide (1·00 g.; α_D^{19} −56·95°, *l* 0·5) in carbon tetrachloride (to 10 ml.) had α_D^{19} −4·05° (*l* 0·5); silver bromide (2·00 g., freshly prepared) was added, and the whole heated with shaking at 73·4°. After 1 hour the solution had α_D^{19} −3·13°, and after 3 further hours α_D^{19} −3·11° (*l* 0·5), 76·8% of the initial value, and on evaporation gave (−)-1-phenylethyl bromide having α_D^{19} −44·18° (*l* 0·5), 77·6% of the original value. A similar experiment employing another specimen of freshly-prepared silver bromide, in which heating was continued for 2 hours, gave 1-phenylethyl bromide having 60·6% of the initial rotatory power. From an experiment similar to the last but employing 3-months aged silver bromide (0·65 g.), (−)-1-phenylethyl bromide (0·8 g.), and carbon tetrachloride (to 8 ml.), the (−)-1-phenylethyl bromide was recovered having 99·9% of the original rotatory power.

Solutions of (+)-1-phenylethyl bromide (2·00 g.) in carbon tetrachloride (to 20 ml.) suffered no racemisation on heating at 73·4° for 2 hours alone and with (*a*) powdered glass (2·00 g.), (*b*) potassium bromide (2·00 g.), or (*c*) styrene dibromide (1·00 g.); on addition of charcoal (0·67 g.) to such a solution the rotatory power fell to 77·0% of the initial rotatory power, but this was due to adsorption since the (+)-1-phenylethyl bromide recovered on evaporation was unchanged in rotatory power. On addition of silica to a similar solution of (−)-1-phenylethyl bromide, the silica swelled and became dark red. The rotation of the solution fell rapidly and became zero after 2 hours. Neither the solution, on evaporation, nor the silica, on heating to 200°/24 mm., yielded any 1-phenylethyl bromide.

Carbon tetrachloride was placed in a 3-necked flask fitted with an inlet tube passing below the surface of the liquid, an exit tube, and a conductivity cell of the dipping type. The resistance of the carbon tetrachloride, measured with a Mullard bridge, was approximately $1·1 \times 10^7$ ohms at 25°; this value remained unchanged when (*a*) the flask was kept at 73·4°, (*b*) the carbon tetrachloride was saturated at 73·4° with hydrogen bromide by passing the latter at 2·8 g./hour for 30 minutes, (*c*) hydrogen bromide was passed continuously at 73·4°, or (*d*) the carbon tetrachloride was saturated with hydrogen bromide at 25°.

Hydrogen bromide was passed at 4·8 g./hour for 30 minutes into carbon tetrachloride (50 ml.) at 73·4°; 20 ml. of the saturated solution were added to water (50 ml.) and titrated with standard sodium hydroxide. The determination was twice repeated with fresh solvent, and similar determinations were made at 25°. Solubility of hydrogen bromide in carbon tetrachloride : at 25°, 0·87, 0·85, 0·90 g./100 ml. of solution; at 73·4°, 0·106, 0·109, 0·108 g./100 ml. of solution.

Thanks are expressed to Dr. J. Kenyon, F.R.S., for his interest in this work and to the Department of Scientific and Industrial Research for a maintenance grant (to G. V. B.).

BATTERSEA POLYTECHNIC, LONDON, S.W.11. [*Received, February 6th*, 1951.]

358. *The Colour of Organic Compounds. Part III.* A New Method of Assessing the ±M Effect of Heterocyclic Nuclei.*

By E. B. Knott and L. A. Williams.

It is shown that the $\pm M$ effects of various heterocyclic nuclei found in cyanine dyes may, with certain exceptions, be assessed in order of increasing strength by a consideration of the absorption shifts resulting on replacement of methin groups by nitrogen atoms in the chromophoric chain of dyes containing these nuclei.

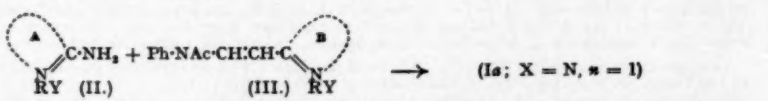
Brooker (*Rev. Mod. Physics*, 1942, **14**, 275; "Advances in Nuclear and Theoretical Organic Chemistry," Interscience Publ. Inc., New York, 1945, Chap. 4) has shown that the $\pm M$ effects of the heterocyclic nuclei contained in cyanine dyes may be set in the order of their relative strengths by his "deviation" method. A second method has now been established which uses as its basis the absorption shift resulting on the replacement of a methin group by a nitrogen atom in the chromophoric system of certain dyes and intermediates.

In Part I (*J.*, 1951, 1024) it was suggested, on the basis of a general rule, that the hypsochromic shift resulting from the replacement of X = CH by X = N in (I*a*; $n = 0$) was primarily caused by the resulting increased significance of the excited structure (I*b*; $n = 0$). In order that the

(I*a*.) (I*b*.)

latter structure may contribute to the resonance hybrid, charge separation is required and the necessary energy involved is offset by the gain in resonance energy of the nucleus (B) on acquiring an additional double bond. Since the latter free-energy change is a function of the $-M$ effect of this nucleus it would be expected that the significance of (I*b*) and the hypsochromic shift experienced in this structural change would increase with increasing $-M$ effect of the nucleus (B).

Table I illustrates this effect in the carbocyanine series, in each set of which nucleus A is constant. The nuclei are given in the order given by Brooker (*loc. cit.*), *i.e.*, of ascending $-M$ effect ("basicity") on proceeding down the table. In general, the order is in fair agreement with that found by Brooker. The exceptions are shown by the low values of the shift for the 1-ethyl-2-quinoline and, in one case, of the 1-ethyl-2-pyridine nuclei, the high value for the 3-ethyl-4-methylthiazole nucleus in the second set, and the reversed order of benzothiazole and benzoselenazole.



(II.) (III.) (I*a*; X = N, $n = 1$)

The required α-azacarbocyanines were readily obtained by condensing the amino-quaternary salt (II) with the required acetanilidovinyl derivative (III).

(IV.) (V.)

In the cyanine series it is found that the shift in the absorption maximum of (IV) on replacing X = CH (max., 422 mμ.) by X = N (max., 368 mμ.) is less (54 mμ.) than in the case of (V) (X = CH, max. = 522 mμ.; X = N, max. = 424 mμ.; Hamer, *J.*, 1924, **125**, 1348), *i.e.*, 98 mμ. Although this is consistent with the higher $-M$ effect of the nuclei in (V) (cf. Brooker) the reverse is true in the carbocyanine series (Table I; cf. Table II). It would appear therefore that in the latter

* Part II, *J.*, 1951, 1028.

TABLE I.

(Ia); $\lambda_{max.}$ (mμ.) *in methanol.*

Nucleus B.	Nucleus A, 3-Ethylbenzothiazole. No.	X = CH.	X = N.	Shift.	Nucleus A, 1-Ethyl-2-quinoline. No.	X = CH.	X = N.	Shift.
1 : 3 : 3-Trimethylindolenine	I	536	478	58	XI	550	483	67
3-Ethylthiazoline	II	502	427	75	XII	526	446	80
3-Ethylbenzoxazole	III	521 *	449	72	XIII	545 *	464	81
3-Ethylbenzoselenazole	V	562 *	466	96	XV	582 *	486	96
3-Ethylbenzothiazole	IV	557 *	465	92	XIV	578 †	489	89
3-Ethylnaphtho(1′ : 2′-4 : 5)thiazole	VI	577 *	483	94	XVI	600 *	496	104
1-Ethyl-2-quinoline	VIII	578 †	488	90	XVIII	605 *	519	86
3-Ethyl-4-methylthiazole	VII	550	448	102	XVII	583	460	123
1-Ethyl-4-quinoline	IX	630 *	513	117	XIX	656 *	555	101
1-Ethyl-2-pyridine	X	535	427	108	XX	578	468	110

Nucleus B.	Nucleus A, 3-Ethyl-4-methylthiazole. No.	X = CH.	X = N.	Shift.
1 : 3 : 3-Trimethylindolenine	XXI	516	469	47
3-Ethylthiazoline	XXII	493	427	66
3-Ethylbenzoxazole	XXIII	508	439	69
3-Ethylbenzoselenazole	XXV	554	473	81
3-Ethylbenzothiazole	XXIV	550	472	78
3-Ethylnaphtho(1′ : 2′-4 : 5)thiazole	XXVI	569	489	80
1-Ethyl-2-quinoline	XXVIII	583	500	83
3-Ethyl-4-methylthiazole	XXVII	548	449	99
1-Ethyl-4-quinoline	XXIX	645	534	111
1-Ethyl-2-pyridine	XXX	557	413	144

* Beilenson, Fisher, and Hamer, *Proc. Roy. Soc.*, 1937, **163**, 138.
† Brooker and Sprague, *J. Amer. Chem. Soc.*, 1941, **63**, 3203.

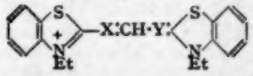
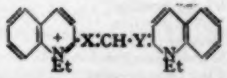
TABLE II.

$\lambda_{max.}$ (mμ.).

Dye.	X = Y = CH.	X = CH, Y = N.	X = Y = N.	Shift Y = CH → Y = N.	Shift X = CH, Y = N → X = Y = N.
VI	557	465	370	92	95
VII	605	519	430 *	86	89

* Fisher and Hamer, *J.*, 1937, 907, give $\lambda_{max.}$ = 343 mμ.

series the shift given by dyes containing a quinoline nucleus is anomalous. This is further illustrated on replacement of a second methin group by nitrogen, as in (VI) and (VII). Table II shows that the replacement shift on replacing each methin group in turn is roughly constant in each series but greater for (VI) than for (VII).

(VI.)   (VII.)

Similar considerations may be applied to the case of the β-anilinovinyl derivatives (VIII; X = CH) and the β-aza-analogues (VIII; X = N). In this case, however, the most likely excited structure (see Part I, *loc. cit.*) involves $-\overset{+}{X}-$ and not $-\overset{-}{X}=$ as in (I), so that the replacement

(VIIIa.) ⟷ (VIIIb.)

of X = CH by X = N will result in a bathochromic shift. The significance of structure (VIIIb) will thus decrease with increasing $-M$ effect of the heterocyclic nucleus, so that the larger shift in this case should be given by the nucleus with the weaker $-M$ effect. Table III shows this to be true.

If in the molecule of (I*a*; X = N) the central chain atom is replaced by nitrogen the azo-compound (IX*a*; X = N) results. As in the case of (VIII), since structures involving $-\overset{+}{X}-$ (*i.e.*, IX*b*) will be more important than those involving $-\overset{-}{X}-$, the replacement shift will be

bathochromic. The magnitude of the shift will similarly decrease with decreasing $+M$ effect (increasing $-M$ effect) of the nucleus A. Table IV shows this to be the case.

Again it is found that the $+M$ effect of the 3-ethylbenzothiazolium nucleus is weaker than that of the selenium analogue (cf. Brooker, *loc. cit.*).

TABLE III.

(VIII); $\lambda_{max.}$ (mμ.) *in methanol.*

Nucleus A.	X = CH.	X = N.	Shift.
1 : 3 : 3-Trimethylindolenine	409	438	29
1-Ethyl-2-quinoline	443	463	20
1-Ethyl-2-pyridine	412	423	11
1-Ethyl-4-quinoline	484	490	6
1-Ethyl-4-pyridine	427	432	5

TABLE IV.

(IX); $\lambda_{max.}$ (mμ.) *in methanol.*

Nucleus A.	X = CH.	X = N.*	Shift.
3-Ethylbenzothiazole	465	495	30
3-Ethylbenzoselenazole	466	486	20
1-Ethyl-2-quinoline	488	497	9

* Fisher and Hamer, *loc. cit.*, give 480, 486, and 480 mμ. respectively.

TABLE V.

Dye (X = N; Table I).	Appearance.	M. p.	Formula.	Found, %. N.	Found, %. I.	Required, %. N.	Required, %. I.
I	Magenta plates *	225°	$C_{22}H_{24}O_4N_2ClS$ [1]	9·15	—	9·1	—
II	Yellow needles	224	$C_{14}H_{20}N_2S_2I$	9·6	28·5	9·45	28·55
III	Orange needles	232	$C_{20}H_{20}ON_2SI$	8·85	25·8	8·8	26·6
IV	Brown needles	268	$C_{20}H_{20}N_2S_2I$	—	25·5	—	25·8
V	Flat rust-coloured needles	278	$C_{20}H_{20}N_2SSeI$	—	23·2	—	23·5
VI	Green crystals	248	$C_{24}H_{22}N_2S_2I$	—	23·7	—	23·4
VII	Orange-brown prisms	257	$C_{17}H_{20}N_2S_2I$	—	28·1	—	27·8
VIII	Flat blue needles	228	$C_{22}H_{22}N_2SI$	—	26·3	—	26·1
IX	Red needles	240	$C_{22}H_{22}N_2SI$	—	26·2	—	26·1
X	Orange crystals *	215	$C_{14}H_{20}O_4N_2SCl$	10·2	—	10·3	—
XI	Red needles *	217	$C_{24}H_{24}O_4N_2Cl$	8·8	—	9·25	—
XII	Orange tablets	205	$C_{18}H_{22}N_2SI$	—	29·3	—	28·9
XIII	Orange needles	249	$C_{22}H_{23}ON_2I$	—	27·3	—	27·0
XIV	Violet needles	271	$C_{22}H_{22}N_2SI$	8·45	26·2	8·65	26·1
XV	Violet needles	267	$C_{22}H_{22}N_2SeI$ [2]	—	24·3	—	23·8
XVI	Bronze crystals	253	$C_{26}H_{24}N_2SI$	7·95	24·4	7·85	23·65
XVII	Garnet needles	230	$C_{19}H_{23}N_2SI$	—	27·8	—	28·15
XVIII	Flat blue needles	263	$C_{24}H_{24}N_2I$	7·85	25·8	7·55	26·4
XIX	Dark red needles	100—101	$C_{24}H_{24}N_2I,C_2H_5{\cdot}OH$ [3]	—	23·8	—	24·1
XX	Red needles *	237	$C_{20}H_{24}O_4N_2Cl$	10·4	—	10·4	—
XXI	Blue plates *	211	$C_{19}H_{24}O_4N_2SCl$	9·65	—	9·85	—
XXII	Long orange needles	250	$C_{13}H_{20}N_2SI$	9·9	—	10·25	—
XXIII	Small orange needles	203	$C_{17}H_{20}ON_2SI,3MeOH$	7·65	—	7·80	—
XXIV	Red amorphous powder	252	$C_{17}H_{20}N_2S_2I$	9·0	—	9·25	—
XXV	Maroon needles	263 (dec.)	$C_{17}H_{20}N_2SSeI$	7·85	—	8·3	—
XXVI	Brown needles	239	$C_{21}H_{22}N_2S_2I$	8·0	—	8·3	—
XXVII	Small maroon crystals	220 (dec.)	$C_{14}H_{20}N_2S_2I$	9·6	—	10·0	—
XXVIII	Brown powder *	225	$C_{19}H_{23}O_4N_2SCl$	9·8	—	9·9	—
XXIX	Green needles	219	$C_{19}H_{23}N_2SI$	9·6	—	9·3	—
XXX	Yellow plates	161	$C_{15}H_{20}O_4N_2SCl,3EtOH$ [4]	8·0	—	8·2	—

* Perchlorates. The remainder are iodides.

[1] Found: C, 57·5; H, 5·1. Reqd.: C, 57·3; H, 5·2%. [2] Found: C, 49·2; H, 4·05. Reqd.: C, 49·5; H, 4·1%. [3] Found: C, 59·6; H, 5·4. Reqd.: C, 59·25; H, 5·7%. [4] Found: C, 49·55; H, 6·4. Reqd.: C, 50·0; H, 6·35%.

Experimental.

Microanalyses by Drs. Weiler and Strauss, Oxford.

α-Azacarbocyanines.—The general procedure adopted was to reflux the 2(or 4)-amino-quaternary salt (1 mol.) with the β-acetanilidovinyl derivative (1 mol.) in ethanol with triethylamine (1 mol.). The dye was then isolated by conversion, if necessary, into the iodide or perchlorate. Unless otherwise stated the dye was recrystallized several times from ethanol or methanol. They are all more soluble than the corresponding carbocyanines which in some cases were formed as by-products. The products are recorded in Table V.

β-Anilino-β-azavinyl Quaternary Salts (VIII*a*; X = N).—Three of these compounds were obtained by Kaufmann and Valette's method (*Ber.*, 1912, **45**, 1736). A more direct method is given below.

2-β-Anilino-β-azavinylquinoline ethiodide. Quinaldine ethiodide (1·5 g.), diazoaminobenzene (1·0 g.), and ethanol (10 c.c.) were refluxed for 10 minutes. The required compound separated (85%) and formed orange-red needles, m. p. 252°, from ethanol (Found: I, 31·35. Calc. for $C_{18}H_{18}N_2I$: I, 31·5%). It was identical with a specimen obtained from 2-formylquinoline ethiodide and phenylhydrazine.

2-β-Anilino-β-azavinyl-3 : 3-dimethylindolenine methiodide. 2 : 3 : 3-Trimethylindolenine methiodide (1·5 g.), diazoaminobenzene (1·55 g.), and ethanol (20 c.c.) were refluxed for 2 minutes. The *dye* (1·2 g.) crystallized on cooling and formed red platelets, m. p. 237°, from ethanol (Found: N, 9·95; I, 31·55. $C_{18}H_{20}N_2I$ requires N, 10·35; I, 31·37%).

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359. *The Catalysed Transfer of Hydrogen Chloride from Chlorohydrins to Epoxides. A New Method of Preparing Glycidol and Some of its Derivatives.*

By William Bradley, James Forrest, and Oliver Stephenson.

Experiments are described on the condensation of epichlorohydrin with phenols to form 1-aryloxy-3-chloropropan-2-ols. The reaction is catalysed by bases, pyridine being the most useful catalyst. The reaction furnishes two by-products, αγ-dichlorohydrin and an αα′-diaryl ether of glycerol. It has been found that the transfer of hydrogen chloride from a chlorohydrin to an epoxide takes place readily in the presence of catalysts. The 1-aryloxy-3-chloropropanols first produced lose hydrogen chloride to form aryl glycide ethers. The liberated hydrogen chloride combines with epichlorohydrin to form αγ-dichlorohydrin, and the aryl glycide ethers combine with the phenols to form αα′-diaryl ethers of glycerol. The mode of reaction of the catalysts is discussed. Several applications of the hydrogen chloride transfer reaction are described in the preparation of glycidol and its derivatives.

The condensation of phenols with epichlorohydrin to form 1-aryloxy-3-chloropropan-2-ols (I) has been studied by many authors. Lindemann (*Ber.*, 1891, **24**, 2145) obtained these products in poor yield by heating a mixture of the two reactants. Later, Boyd and Marle (*J.*, 1910, **97**, 1788) and Marle (*J.*, 1912, **101**, 305) improved the yields by carrying out the condensation in the presence of sodium hydroxide at room temperature for a period of six weeks. More recently, Levas and Lefebre (*Compt. rend.*, 1946, **222**, 555, 1439) have employed boron trifluoride, a reagent which necessitates the use of a large excess of the phenols if the 1-aryloxy-3-chloropropan-2-ols are to be prepared in good yield. Several authors (Lindemann, *loc. cit.*; Boyd and Marle, *J.*, 1908, **93**, 838; 1909, **95**, 1807) have reported the formation of αα′-diaryl ethers of glycerol (III) as by-products.

$$\mathrm{ArOH} + \mathrm{CH_2{-}\overset{O}{\overset{\diagup\diagdown}{}}{-}CH{\cdot}CH_2Cl} \longrightarrow \mathrm{ArO{\cdot}CH_2{\cdot}CH(OH){\cdot}CH_2Cl} \quad \text{(I.)}$$

$$\text{(II.)} \quad \mathrm{ArO{\cdot}CH_2{\cdot}CH{-}\overset{O}{\overset{\diagup\diagdown}{}}{-}CH_2} \xrightarrow{\mathrm{ArOH}} \mathrm{ArO{\cdot}CH_2{\cdot}CH(OH){\cdot}CH_2{\cdot}OAr} \quad \text{(III.)}$$

The readiness of alkali phenoxides to combine with epichlorohydrin harmonizes with a number of observations which have shown that anions react easily with α-epoxides. Sodiomalonic ester (Traube and Lehmann, *Ber.*, 1899, **32**, 720; 1901, **34**, 1971; Haller and Blanc, *Compt. rend.*, 1906, **142**, 1471; Kotz and Hoffmann, *J. pr. Chem.*, 1925, **110**, 105), sodium hydrogen sulphite

(Erlenmeyer, *Z. Chem.*, 1868, **342**; Darmstadter, *Annalen*, 1868, **148**, 125; Brunel, *Compt. rend.*, 1903, **137**, 63), and sodium thiosulphate (Ross, *J.*, 1950, 2257) all react additively with α-epoxides and the same is likely to be true of phenoxide ions.

The present study of the condensation of phenols with epichlorohydrin has shown that tertiary amines, *e.g.*, pyridine and triethylamine, are suitable catalysts for the reaction. Primary and secondary amines also may be used but offer no advantages. Good results are obtained by employing the reactants in equimolecular proportions and adding the tertiary amines in amounts equivalent to 0·2—1·0% of the combined weight. At 90—95° the 1-aryloxy-3-chloropropan-2-ols are obtained in 50—70% of the theoretical yield after 4—10 hours' heating. The results compare favourably with the optimum yields of Boyd and Marle (*J.*, 1910, **97**, 1778) and Marle (*loc. cit.*), who obtained yields of 26% and 60—70% after keeping the reactants at room temperatures for 21 and 40—60 days, respectively. As in the older methods of preparation, by-products are formed, the proportion increasing with increase in the proportion of the tertiary base.

The more acidic phenols combine more readily than the weaker with epichlorohydrin. This result is to be expected if the relative concentration of the various phenoxide ions in the reaction mixture is the most important consideration, but the relative reactivities of the phenoxide anions towards epichlorohydrin must also be involved. In this connection Brønsted, Kilpatrick, and Kilpatrick (*J. Amer. Chem. Soc.*, 1929, **51**, 428) observed the following anions to be in order of increasing reactivity towards epichlorohydrin, formate < benzoate < acetate < chloride < bromide < iodide. The anions of the halogen hydracids were more effective than any derived from the weaker organic acids, but within the series of organic anions the anion of the weakest acid was the most effective. The greater reactivity of the more strongly acidic phenols was reflected in the higher yields of 1-aryloxy-3-chloropropan-2-ols obtained by their use.

Whichever condensing agent is employed, the reaction product contains the αα′-diaryl ethers (III). Table I (p. 1594) summarises the yields of (I) and (III), expressed as percentages of the theoretical, when various phenols are condensed with equimolecular amounts of epichlorohydrin; the amounts of catalyst are expressed as percentages of the combined weights of the reactants.

The yields of the 1-aryloxy-3-chloropropan-2-ols are uniformly higher than those of the related αα′-diaryl ethers of glycerol. It appeared that hydrogen chloride was lost from the chlorohydrins, yielding the 1-aryloxy-2 : 3-epoxypropanes (II), which then reacted additively with phenols. The formation of epoxides such as (II) from chlorohydrins (I), however, was believed to require the use of strong alkalis.

Two observations have now been made which suggest the correctness of the second hypothesis; both αγ-dichlorohydrin and the epoxides (II) can be isolated from the reaction products. For example, the condensation of epichlorohydrin with β-naphthol yields 1-chloro-3-naphthoxypropane-2-ol and αγ-dichlorohydrin; phenol and epichlorohydrin yield 1-chloro-3-phenoxypropane-2-ol, glycide phenyl ether, 1 : 3-diphenoxypropan-2-ol, and αγ-dichlorohydrin.

The dichlorohydrin could only have resulted by the addition of hydrogen chloride to epichlorohydrin, and glycide phenyl ether only by loss of hydrogen chloride from 1-chloro-3-phenoxypropan-2-ol. It appeared possible that the two reactions were related, epichlorohydrin acting as a hydrogen chloride acceptor and 1-chloro-3-phenoxypropan-2-ol as a hydrogen chloride donor.

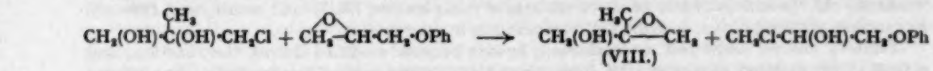
Experiment has shown that the transfer of hydrogen chloride from chlorohydrins to epoxides takes place readily in many instances under appropriate conditions, a new epoxide and chlorohydrin resulting.

$$\underset{\text{(IV.)}}{RO{\cdot}CH_2{\cdot}CH(OH){\cdot}CH_2Cl} + \underset{\text{(V.)}}{R'O{\cdot}CH_2{\cdot}\overset{\overset{O}{\diagup\diagdown}}{CH}{-}CH_2} \rightleftharpoons \underset{\text{(VI.)}}{RO{\cdot}CH_2{\cdot}\overset{\overset{O}{\diagup\diagdown}}{CH}{-}CH_2} + \underset{\text{(VII.)}}{R'O{\cdot}CH_2{\cdot}CH(OH){\cdot}CH_2Cl}$$

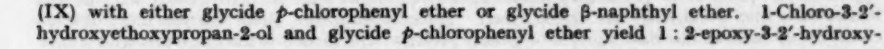
When α-monochlorohydrin (IV; R = H) is heated with glycide phenyl ether (V; R′ = Ph) and the product is fractionally distilled, glycidol (VI; R = H) and 1-chloro-3-phenoxypropan-2-ol (VII; R′ = Ph) are obtained. Similarly, glycidol results together with a 1-chloro-3-aryloxypropan-2-ol when α-monochlorohydrin is heated with glycide *o*-tolyl ether, glycide *p*-tolyl ether, or glycide *p*-chlorophenyl ether. An analogous reaction occurs between monochlorohydrin and quinol bisglycide ether. Under appropriate conditions the yield of glycidol exceeds 95% of the theoretical.

The transfer of hydrogen chloride from a chlorohydrin to an epoxide has enabled many derivatives and analogues of glycidol to be prepared conveniently. β-Methylglycidol (VIII) results by heating 3-chloro*iso*butane-1 : 2-diol with glycide phenyl ether. *O*-Acetylglycidol is

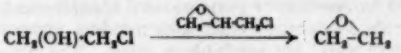
formed by heating 1-acetoxy-3-chloropropan-2-ol with glycide *p*-chlorophenyl ether. Glycide 2-hydroxyethyl ether (X) is produced by heating 1-chloro-3-2′-hydroxyethoxypropan-2-ol

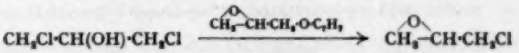


(IX) with either glycide *p*-chlorophenyl ether or glycide β-naphthyl ether. 1-Chloro-3-2′-hydroxyethoxypropan-2-ol and glycide *p*-chlorophenyl ether yield 1 : 2-epoxy-3-2′-hydroxy-



ethoxypropane. This was characterised by combining it with *o*-cresol to give 1-2′-hydroxyethoxy-3-*o*-tolyloxypropan-2-ol. Aryl ethers of glycidol can be prepared by similar processes. 1-Chloro-3-*o*-tolyloxypropan-2-ol, heated with either glycide β-naphthyl ether or *p*-phenylene bisglycide ether, yields glycide *o*-tolyl ether Epichlorohydrin results when glycerol αγ-dichlorohydrin is heated with glycide *o*-tolyl ether; ethylene oxide by heating ethylene chlorohydrin with epichlorohydrin:

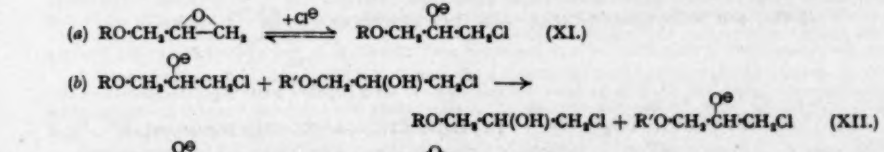




The process of hydrogen chloride transfer is not limited to 1 : 2-chlorohydrins. For example heating with glycide phenyl ether transforms 3-bromopropan-1-ol into 1 : 3-epoxypropane (oxetane).

The method enables a number of difficultly accessible epoxides to be prepared from the more readily accessible. The most satisfactory procedure is to mix the chlorohydrin related to the epoxide to be prepared with an epoxide of higher boiling point to function as a hydrogen chloride acceptor. The mixture of chlorohydrin and epoxide is heated and then distilled slowly through an efficient column at an appropriate pressure. The epoxide produced as a result of the reaction distils, leaving behind a chlorohydrin related to the original epoxide reactant. Propylene oxide is conveniently prepared at atmospheric pressure. Glycidol and its simple derivatives are preferably distilled at 10—20 mm. Lower pressures are desirable when the product is a glycide aryl ether. In all the instances investigated the transfer of hydrogen chloride required the presence of a catalyst. Aqueous ammonia, primary and secondary amines such as aniline and piperidine, potassium hydroxide, and potassium carbonate were effective, but tertiary amines such as pyridine, quinoline, and triethylamine were more satisfactory. The most successful catalysts giving the highest rate of transfer were quaternary ammonium salts such as pyridinium ethiodide, *p*-nitrobenzylpyridinium bromide, and 2′ : 3′-dihydroxypropylpyridinium chloride. Table II (p. 1596) summarises the results of several interchange reactions employing various chlorohydrins and epoxides and a range of catalysts. On p. 1595 are summarised results which show the influence of conditions on the progress of one reaction, *viz.*, that between *p*-chlorophenyl glycide ether (2 mols.) and α-monochlorohydrin (1 mol.), which yields glycidol as the volatile product in 0—98% of the theoretical yield, calculated on the α-monochlorohydrin employed.

When the catalyst is a quaternary ammonium salt it is always recoverable unchanged from the product of the reaction. The efficiency of the salts as catalysts recalls the experiments of Brønsted, Kilpatrick, and Kilpatrick (*loc. cit.*) in which the reactivity of epoxides towards halide ions was demonstrated. It would appear that their content of halide ions is important, even

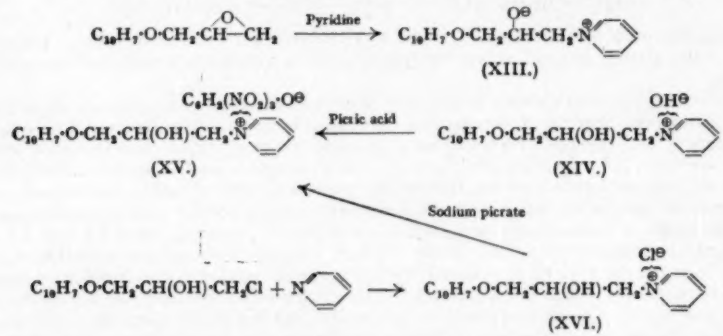


if not essential, to the catalytic activity of the quaternary salts. Hammett ("Physical Organic Chemistry," McGraw-Hill Book Co. Inc., p. 301) has postulated the formation of a

complex ion (XI), and it may be expected that such would be in equilibrium with the epoxide and react with one or more of the hydroxylated compounds present, *e.g.*, the chlorohydrin reactant. If the chlorohydrin is involved a new complex ion (XII) will result, and this will decompose, yielding a new epoxide and regenerating a chloride ion.

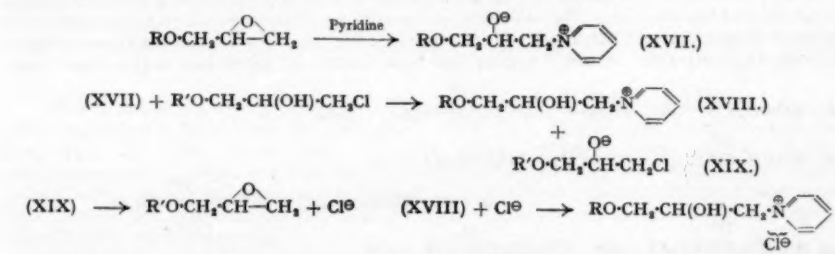
Tertiary amines employed as condensing agents become modified during the reaction, and appear in the product as quaternary ammonium salts; some part of their activity may be due to the salts into which they are transformed. Initially, however, their reaction must involve either the epoxide or the chlorohydrin originally present: the former is the more probable course for the following reasons. In separate experiments it has been shown that the rate of reaction of the chlorohydrins with pyridine is slow, even at high temperatures. By comparison, the rate of reaction of pyridine with epoxides is rapid. Finally, the quaternary salts formed during the reaction are related to the epoxide originally present, not to the chlorohydrin reactant. For example, in the reaction between α-monochlorohydrin and glycide phenyl ether catalysed by pyridine, the base is transformed into 2′-hydroxy-3′-phenoxypropylpyridinium chloride. Only when the molecular concentration of the pyridine approaches that of the epoxide and chlorohydrin reactant are two quaternary salts isolable.

The products obtained by reaction of pyridine with epoxides had the character of internal salts. For example, glycide β-naphthyl ether and pyridine yielded a product, regarded as (XIII), which was soluble in water but insoluble in ether. The aqueous solution, mixed with sodium picrate or picric acid, precipitated 2′-hydroxy-3′-β-naphthoxypropylpyridinium



picrate (XV), identical with the product obtained by reaction of 2′-hydroxy-3′-β-naphthoxypropylpyridinium chloride (XVI) with sodium picrate. Mixed with hydrochloric acid, the aqueous solution yielded 2′-hydroxy-3′-β-naphthoxypropylpyridinium chloride directly. The chloride so formed was identical with the salt obtained by combining pyridine with 1-chloro-3-β-naphthoxypropan-2-ol. It appears that the aqueous solution of the epoxide–pyridine adduct contains the internal salt (XIII) or the related 'onium hydroxide (XIV), or both of these forms.

The catalytic action of pyridine in promoting the transfer of hydrogen chloride from a chlorohydrin to an epoxide may therefore involve the following stages:



Experiments on the character and yield of the quaternary salts isolable from epoxide–chlorohydrin mixtures after they had been heated with pyridine are summarised in Table III.

The results show that when relatively large amounts of pyridine are used the yields of quaternary salts increase markedly with time of heating, and with increase in the proportion of epoxide reactant. Reduction in the proportion of pyridine increases the yields of isolable homogeneous quaternary salts, probably for the reason that with small amounts of pyridine reaction is mainly confined to the formation of one of the two possible salts, which individual is then more easily isolated. The properties of the quaternary chlorides and picrates encountered in these experiments are summarised on pp. 1595, 1597.

Pyridine ethiodide employed as a catalyst in the reaction of epoxides with chlorohydrins was recovered in its original form. The iodide was expected to be more reactive than the chloride in view of the results of Brønsted *et al.* (*loc. cit.*) but the ultimate presence of iodide in the product suggests that the iodide has a lower solubility than the chloride.

The catalytic activity of alkali hydroxides and carbonates probably depends on their ability to liberate chloride ions from the chlorohydrin constituent; these bases are, in fact, changed into alkali chlorides during the reaction. Preformed sodium and potassium chloride have little or no catalytic action, probably because of their insolubility in the reagents. Hydrogen chloride exerts a catalytic effect which is less marked than that of pyridine or pyridinium ethiodide. In this instance chloride ions are present initially, but some become combined with the epoxide reactant, yielding a chlorohydrin, and are not replaced:

$$HCl + >C\overset{O}{\frown}CH_2 \longrightarrow >C(OH)\cdot CH_2Cl$$

The rate of transfer of hydrogen chloride increased with the proportion of catalyst employed. When tertiary amines or quaternary ammonium halides were used, 0·02—0·04 mol. of the catalyst per 100 g. of total reactants afforded a convenient rate of transfer. In preparing epoxides that were prone to polymerise, it was important to ensure that the distillate was free from catalyst. In these instances the use of the quaternary ammonium halides was preferred. Alternatively, when tertiary amines were employed the reaction product was heated for some time before distillation to ensure complete conversion of the tertiary base into a non-volatile quaternary ammonium salt.

The preparation of anhydrous glycidol is of considerable practical interest. A convenient method affording almost theoretical yields consists in heating α-monochlorohydrin with a glycide aryl ether in the presence of pyridine or its ethiodide. This procedure may be contrasted with the earlier preparation by Nivière (*Bull. Soc. chim.*, 1914, **15**, 464) in which a solution of α-monochlorohydrin in ether is treated with sodium.

The present investigation throws light on the mode of formation of the dichlorohydrin observed by Lespieaux (*ibid.*, 1905, **33**, 462) as a by-product of the reaction between epichlorohydrin and hydrogen cyanide. In this reaction chlorine is eliminated, presumably as chloride ion, and the further reaction of this with epichlorohydrin must lead to dichlorohydrin.

Experimental.

Condensation of p-*Chlorophenol with Epichlorohydrin. Formation of* 1-*Chloro*-3-p-*chlorophenoxypropan*-2-*ol and Glycerol* αα′-*Di*-p-*chlorophenyl Ether.*—(1) *p*-Chlorophenol (112 g.), epichlorohydrin (81 g.), and 40% aqueous sodium hydroxide (1 c.c.) were mixed and kept at room temperature for 45 days. The product was made just acid with acetic acid, washed with water, dried (Na_2SO_4), and then distilled. The following fractions were collected; (*a*) b. p. up to 144°/1 mm. (12·1 g.); (*b*) b. p. 144—148°/1 mm. (148 g.). There was only a trace of a residue. The second fraction (Found, on hydrolysis: Cl′, 15·9. Calc. for $C_9H_{10}O_2Cl_2$: Cl′, 16·1%) was almost pure 1-chloro-3-*p*-chlorophenoxypropan-2-ol.

(2) When the reactants employed in (1) were heated under reflux for 24 hours instead of being kept at the room temperature, and the product was then distilled, a fraction, b. p. 138—140°/0·5 mm. (94 g.) was obtained. It consisted mainly of 1-chloro-3-*p*-chlorophenoxypropan-2-ol (yield, 52%). Its composition was proved by hydrolysing it to glycerol α-*p*-chlorophenyl ether. This fraction (22·1 g. of redistilled material, b. p. 138°/0·5 mm.) was heated under reflux during 5 hours with a solution of potassium carbonate (13·8 g.) in water (200 c.c.). After cooling, the solid product was collected, washed with water, and dried (yield 19·5 g.; m. p. 72—74°). Recrystallisation from carbon tetrachloride gave glycerol α-*p*-chlorophenyl ether, m. p. 76—78°, not depressed by admixture with an authentic specimen.

A minor fraction, b. p. 200—230°/0·5—1 mm. (21 g.), triturated with ether–light petroleum, gave a white, crystalline solid (19 g.) which after recrystallisation from ether–light petroleum afforded hard white prisms of glycerol αα′-*di*-p-*chlorophenyl ether*, m. p. 89—90° (Found: C, 57·5; H, 4·7; Cl, 22·4. $C_{15}H_{14}O_3Cl_2$ requires C, 57·5; H, 4·5; Cl, 22·7%).

Condensation of β-*Naphthol with Epichlorohydrin. Formation of* αγ-*Dichlorohydrin.*—A suspension containing β-naphthol (54 g.) and epichlorohydrin (38·2 g.) in benzene (80 c.c.) was heated until it became homogeneous. Pyridine (1 c.c.) was then added, and the heating continued at 80—90° for 20 hours. The solvent was distilled off, the last portions under somewhat reduced pressure. The residue was distilled, and a fraction, b. p. *ca.* 100°/12 mm., was collected, dried ($MgSO_4$), and redistilled at atmospheric

pressure. The main fraction, b. p. 160—175°, weighed 5·8 g. A few drops mixed with cold, alcoholic sodium hydroxide gave an immediate precipitate of sodium chloride and the characteristic odour of epichlorohydrin. The main portion was shaken with light petroleum (b. p. 40—60°) containing phenyl *iso*cyanate. Clusters of white plates slowly separated, and these, recrystallised from methanol, had m. p. 73°, not depressed when mixed with an authentic specimen of the phenylurethane of αγ-dichlorohydrin.

Condensation of Phenol with Epichlorohydrin. Formation of αγ-Dichlorohydrin and Glycide Phenyl Ether.—Phenol (188 g.), epichlorohydrin (194 g.), and pyridine (2 g.) were mixed and heated to 85—90°. An exothermic reaction occurred, necessitating cooling to prevent rise in temperature. The red-brown liquid was heated at 90° for a further 12 hours and then distilled. The following fractions were collected: (*a*) b. p. 85°/3 mm. (75 g.); (*b*) b. p. 90—115°/3 mm. (4 g.); (*c*) b. p. 120—135°/3 mm. (175 g.); (*d*) b. p. 140—185°/3 mm. (20 g.); (*e*) b. p. 185—195°/3 mm. (60 g.). A residue (15 g.) remained. Fraction (*a*), when redistilled, gave a middle fraction, b. p. 176—182°; when this was mixed with cold sodium hydroxide solution, epichlorohydrin, b. p. 117°, was formed. This result indicated the presence of αγ-dichlorohydrin in fraction (*a*). A further portion of fraction (*a*) was warmed with aqueous alcoholic sodium hydroxide and phenol [2 mols., calculated on assumption that fraction (*a*) was αγ-dichlorohydrin]. The reaction yielded glycerol αα′-diphenyl ether, m. p. 81°, not depressed when mixed with the same product prepared from authentic αγ-dichlorohydrin. Fraction (*b*) was redistilled, and a middle fraction, b. p. 89°/1 mm., collected. It was free from chlorine. Its identity as glycide phenyl ether was proved by mixing it with piperidine and crystallising the condensation product from light petroleum (b. p. 60—80°). The adduct formed large colourless needles, m. p. 55° (Found: C, 71·8; H, 8·4; N, 6·1. $C_{14}H_{21}O_2N$ requires C, 71·4; H, 9·0; N, 6·0%), identical with the *1-phenoxy-3-piperidinopropan-2-ol* obtained by combining piperidine with an authentic specimen of glycide phenyl ether. Fraction (*c*) consisted essentially of 1-chloro-3-phenoxypropan-2-ol; the yield was 64% of the theoretical. Fraction

TABLE I.

Ar in ArOH.	Catalyst.	Amount of catalyst.	Reaction: Time.	Reaction: Temp.	Yield, %. Ar·O·CH_2·CH(OH)·CH_2Cl	Yield, %. Ar·O·CH_2·CH(OH)·CH_2·OAr
Phenyl	Na_2CO_3	0·25	24 hours	90°	40	—
	K_2CO_3	0·5	100 ,,	90	54	14
	,,	0·5	4 ,,	90—156	34	14
	,,	0·5	9·5 ,,	90—160	44	21
	Pyridine	0·5	20 ,,	90	46	15
	Quinoline	0·3	43 days	20	55	3
	Triethylamine	0·3	34 ,,	20	59	16·5
	Morpholine	0·4	61 ,,	20	66	12·4
m-Tolyl	Triethylamine	0·5	64 days	20	69	16·5
p-Tolyl	Dimethylaniline	1·0	10 hours	90—105	55	11·4
o-Tolyl	KOH	0·2	10 hours	80—90	24	—
	,,	0·2	65 days	20	36·3	9·5
	K_2CO_3	0·5	15 hours	128—153	17	3·5
	Pyridine	0·5	3 ,,	92—102	22·8	14·0
	Quinoline	1·0	64 days	20	44	7·4
	Dimethylaniline	0·75	3·5 hours	92—100	34	16·5
	,,	1·50	4 ,,	92—113	43·5	24·0
	,,	1·0	10 ,,	90—100	51	12·5
	Aniline *	0·5	64 days	20	18	?
	Triethylamine	0·6	3 hours	92—99	25·5	12·5
	,,	0·6	5·5 ,,	92—109	35	16·2
	Triethanolamine	0·5	3 ,,	92	22·3	7·3
p-Chlorophenyl	NaOH	0·2	45 days	20	76	None
	KOH	1·0	66 ,,	20	76·5	11·2
	Quinoline	0·5	69 ,,	20	78	3
	,,	0·5	64 ,,	20	72·8	5
	,, †	0·3	69 ,,	20	49	?
o-Methoxyphenyl	Pyridine	0·5	68 days	20	64	16
β-Naphthyl	Dimethylaniline ‡	1·7	20 hours	90	60	?

* Two molecular proportions of *o*-cresol were used in this experiment.
† Two molecular proportions of epichlorohydrin were used in this experiment.
‡ In this experiment benzene was used as a diluent.

(*e*) solidified on cooling; recrystallisation from aqueous alcohol afforded lustrous plates, m. p. 80—82°, not depressed on admixture with an authentic specimen of glycerol αα′-diphenyl ether.

In the following experiments various phenols were heated with equimolecular amounts of epichlorohydrin in the presence of catalysts, under the conditions summarised in Table I. The products were distilled, and fractions consisting of the 1-aryloxy-3-chloropropan-2-ols and glycerol αα′-diaryl ethers were collected. The yields are given as percentages of the theoretical. The amounts of the catalysts employed are given as percentages of the total weight of reactants.

Reaction of Glycide Phenyl Ether with α-Monochlorohydrin. Formation of Glycidol.—Glycide phenyl ether (844 g., 1·125 mols.), α-monochlorohydrin (552·5 g., 1·0 mol.), and pyridinium ethiodide (47·5 g.) were mixed and heated under reduced pressure, the volatile products being passed through an efficient fractionating column. Glycidol commenced to distil almost at once. It was collected during 2—3 hours, depending on the rate of distillation, as a fraction, b. p. 60—85°/15 mm. (365 g.). Redistillation gave pure glycidol, b. p. 64—65°/14 mm. (355 g.; 96% of theoretical). The residue, a red-brown, somewhat viscous oil, was distilled through a short Vigreux column. A first fraction, b. p. 120—155°/15 mm. (140 g.), consisted mainly of glycide phenyl ether. This was followed by a fraction, b. p. 156—160°/10—11 mm. (835 g.), consisting of 1-chloro-3-phenoxypropan-2-ol (yield, approx. 90%).

In preparing large amounts of glycidol it was found convenient to reconvert the 1-chloro-3-phenoxypropan-2-ol into glycide phenyl ether for further use by stirring it for 2 hours at 25° with a solution of sodium hydroxide (240 g.) in water (1 l.). By this means glycide phenyl ether was recovered in 92% yield calculated on the 1-chloro-3-phenoxypropan-2-ol treated.

Reaction of Glycide o-Tolyl Ether with α-Monochlorohydrin.—A mixture of glycide *o*-tolyl ether (738 g.), α-monochlorohydrin (442 g.), and pyridine (18 g.) was heated at 60—65° until the odour of pyridine had disappeared (10—15 mins.). Distillation of the product afforded glycidol (272 g., 92%) and 1-chloro-3-*o*-tolyloxypropan-2-ol, b. p. 160—165°/10 mm. (680 g., 85%).

Reaction of Glycide Phenyl Ether and Trimethylene Bromohydrin. Formation of 1 : 3-*Epoxypropane.*—A mixture of propylene bromohydrin (100 g.), glycide phenyl ether (120 g.), and pyridinium ethiodide (6 g.) was heated, and the volatile products were passed through an efficient fractionating column. The first fraction, b. p. 45—55°, was collected during 45 mins. On redistillation it gave propylene oxide (1 : 3-epoxypropane), b. p. 47° (38 g., 92%).

The results of several other experiments on the reaction between epoxides and chlorohydrins are summarised in Table II.

Reaction of Glycide p-Chlorophenyl Ether with 1-Chloro-3-2′-hydroxyethoxypropan-2-ol.—Glycide *p*-chlorophenyl ether (41·8 g.), 1-chloro-3-2′-hydroxyethoxypropan-2-ol (35 g.; Kharasch and Nudenberg, *J. Org. Chem.*, 1943, **8**, 189), and triethylamine (1 c.c.) were mixed and then slowly distilled under reduced pressure. The first portion of the distillate, b. p. 90—96°/1—2 mm. (24 g.), was redistilled. 1 : 2-Epoxy-3-2′-hydroxyethoxypropane, b. p. 72°/0·5 mm., was obtained in a yield of 21 g. The new epoxide was characterised by means of its adduct with *o*-cresol. The epoxide (11·8 g.), *o*-cresol (10·8 g.), and triethylamine (0·2 c.c.) were kept for 3 weeks at room temperature. Distillation under reduced pressure then gave 1-2′-*hydroxyethoxy*-3-*o*-*tolyloxypropan*-2-*ol*, b. p. 175°/0·5 mm. (Found: C, 63·5; H, 8·0. $C_{12}H_{18}O_4$ requires C, 63·7; H, 8·0%), as a colourless, viscous oil (19·5 g., 86%).

A mixture of epichlorohydrin (2 mols.), ethylene chlorohydrin (1 mol.), and pyridinium ethiodide (0·05 mol. per 100 g. of reactants) gave ethylene oxide (0·75 mol.).

Quinol diglycide ether (1 mol.), α-monochlorohydrin (2 mols.), and quinoline (0·015 mol. per 100 g. of reactants) afforded glycidol, b. p. 65°/14 mm. (1·54 mols.). Quinol diglycide ether (1 mol.), 1-chloro-3-*o*-tolyloxypropan-2-ol (2 mols.), and quinoline (0·02 mol. per 100 g. of reactants) yielded glycide *o*-tolyl ether, b. p. 95°/2 mm. (1·0 mol.).

N-(2 : 3-Epoxypropyl)-*N*-methylaniline (1 mol.) and α-monochlorohydrin (1 mol.) reacted without the aid of an added catalyst to yield glycidol, b. p. 65°/14 mm. (0·5 mol.).

Reaction between p-Chlorophenyl Glycide Ether (2 Mols.) and α-Monochlorohydrin (1 Mol.). Influence of Condensing Agent.—A mixture of the reactants with one or other of the catalysts listed below was heated until glycidol ceased to distil. The yields obtained were: pyridine, 93%; quinoline, 92%; triethylamine, 50%; 2′ : 3′-dihydroxypropylpyridinium chloride, 96—98%; 2′-hydroxy-3′-*o*-tolyloxypropylpyridinium chloride, 96—98%; *p*-nitrobenzylpyridinium chloride, 96—98%; pyridine ethiodide, 96—98%; potassium hydroxide, 58—60%; potassium carbonate, 65%; ammonia (*d* 0·88), 92—95%; ammonium chloride, 85%; aniline, 40%; piperidine, 80%; hydrochloric acid (*d* 1·16), 30%. There was almost no reaction in the absence of added catalyst, or on the addition of metallic copper, zinc, or aluminium, or of sodium chloride or potassium chloride. The reaction induced by hydrogen chloride proceeded very slowly; the four quaternary pyridinium salts gave the most rapid rate of change.

The Condensation of Epoxides with Chlorohydrins in the Presence of Pyridine. Formation of Quaternary Salts.—(i) A mixture of glycide *o*-tolyl ether (20·0 g.), 1-chloro-3-*p*-chlorophenoxypropan-2-ol (25·6 g.), and pyridine (4·8 g.) was heated at 60° for 90 mins. The red-brown solution was added to ethyl acetate (250 c.c.), and the precipitate stirred to induce crystallisation. The crude solid (9·5 g.) was extracted thoroughly by means of cold ethyl acetate and then recrystallised from ethyl acetate–methanol. The pure salt formed white needles (8·1 g.), m. p. 163—164° (Found: C, 64·1; H, 6·5; N, 5·0; Cl, 12·5. $C_{11}H_{14}O_3NCl$ requires C, 64·4; H, 6·4; N, 5·0; Cl, 12·7%) not depressed on mixing with authentic 2′-*hydroxy*-3′-*o*-*tolyloxypropylpyridinium chloride* having the same m. p. Admixture with 3′-*p*-chlorophenoxy-2′-hydroxypropylpyridinium chloride depressed the m. p. to 140—150°. 2′-*Hydroxy*-3′-*o*-*tolyloxypropylpyridinium picrate* crystallised from methanol in orange-yellow needles, m. p. 146—147° (Found: N, 12·0. $C_{21}H_{18}O_9N_4$ requires N, 11·9%).

TABLE II.

Ar in epoxide, $CH_2(O)CH\cdot CH_2\cdot OAr$.	Chlorohydrin.	Molar ratio, epoxide : chlorohydrin.	Catalyst.*	Amount of catalyst, mol. per 100 g. of reactants.	Products. Epoxide.	Products. Yield of epoxide, mols.	Products. B. p. of epoxide.	Yield (mols.) of chlorohydrin.†
Ph	α-Monochlorohydrin	1 : 1	C_5H_5N,EtI	0·015	Glycidol	0·75	65°/14 mm.	—
,,	,,	1·15 : 1	,,	0·015	,,	0·95	,,	0·93
o-C_6H_4Me	,,	2 : 1	C_5H_5N	0·0125	,,	0·95	64°/14 mm.	—
,,	,,	1 : 1	,,	0·013	,,	0·68	63—64°/14 mm.	—
,,	,,	1 : 2	,,	0·013	,,	0·95	,,	—
,,	,,	1 : 1	C_9H_7N	0·01	,,	0·62	65°/14 mm.	0·78
,,	,,	1 : 3	,,	0·005	,,	0·85	,,	—
p-C_6H_4Cl	,,	1 : 2	K_2CO_3	0·1	,,	0·65	,,	0·70
p-C_6H_4Me	,,	1 : 1	C_9H_7N	0·015	,,	0·70	,,	—
,,	,,	1 : 2	,,	0·015	,,	0·80	,,	—
Ph	3-Chloro*iso*butane-1 : 2-diol	1·15 : 1	C_5H_5N,EtI	0·015	2 : 3-Epoxy*iso*-butan-1-ol	0·93	63°/12 mm.	0·60
p-C_6H_4Cl	1-Acetoxy-3-chloro-propan-2-ol	1 : 1	C_9H_7N	0·015	*o*-Acetylglycidol	0·61	64°/15 mm.	0·73
β-$C_{10}H_7$	1-Chloro-3-2′-hydroxyethoxypropan-2-ol	1 : 1	NEt_3	0·02	Glycidol 2-hydroxyethyl ether	0·90	94°/2 mm.	—
o-C_6H_4Me	α-Monochlorohydrin	1 : 1	,,	0·011	Glycidol	0·36	65°/14 mm.	0·49
,,	,,	1 : 2	,,	0·011	,,	0·49	,,	0·55
p-C_6H_4Cl	,,	1 : 2	Piperidine	0·007	,,	0·80	,,	0·74
,,	,,	1 : 2	KOH	0·007	,,	0·58	,,	0·76
,,	,,	1 : 2	A	0·014	,,	*ca.* 1·0	,,	0·76
,,	,,	1 : 2	B	0·014	,,	*ca.* 1·0	,,	0·81
,,	,,	1 : 2	K_2CO_3	0·021	,,	0·72	,,	0·74
,,	,,	1 : 2	NH_4Cl	0·007	,,	0·85	,,	0·72
,,	,,	1 : 2	NH_3 (*d* 0·88)	0·007	,,	0·95	,,	0·73
Ph	,,	1 : 1·15	C_5H_5N,EtI	0·010	,,	0·97	,,	0·93
p-C_6H_4Cl	,,	1 : 1	,,	0·02	,,	0·92	72°/0·5 mm.	—
β-$C_{10}H_7$	1-Chloro-3-*o*-tolyloxypropan-2-ol	1 : 2	C_9H_7N	0·02	Glycide *o*-tolyl ether	0·55—0·58	95°/2 mm.	—
o-C_6H_4Me	αγ-Dichlorohydrin	1 : 1	C_5H_5N	0·01	‡ Epichlorohydrin	0·16	120°/760 mm.	—
p-C_6H_4Cl	,,	1 : 1	C_9H_7N	0·015	‡ ,,	0·2—0·3	,,	—

* A = 4-Nitrobenzylpyridinium chloride; B = 2′-hydroxy-3′-*o*-tolyloxypropylpyridinium chloride.
† In these chlorohydrins, $Ar\cdot O\cdot CH_2\cdot CH(OH)\cdot CH_2Cl$, Ar is identical with that in col. 1.
‡ These products contained an undetermined amount of acraldehyde.

(ii) A mixture of glycide phenyl ether (16·2 g.), 1-chloro-3-phenoxypropan-2-ol (20·0 g.), and pyridine (4·3 g.), treated as in (i), yielded 9·7 g. of crude 2′-hydroxy-3′-phenoxypropylpyridinium chloride. Crystallisation from ethyl acetate–methanol afforded rosettes of small needles, m. p. 137—138°. The derived *picrate* crystallised from methanol in hexagonal plates, m. p. 151—152° (Found: N, 12·0. $C_{26}H_{18}O_9N_4$ requires N, 12·2%). The ethyl acetate mother-liquor yielded 14·7 g. of glycide phenyl ether and 7·5 g. of 1-chloro-3-phenoxypropan-2-ol.

(iii) A mixture of glycide β-naphthyl ether (40 g.) and pyridine (7·9 g.) was heated at 60° for an hour. 1-Chloro-3-*o*-tolyloxypropan-2-ol (20 g.) was added, and the mixture kept at 60° for one hour longer. The product was added to dry ether (250 c.c.) and vigorously stirred. The insoluble portion was separated and again stirred with ether. The ethereal solutions were combined, and washed in turn by means of water, 0·02N-hydrochloric acid (250 c.c.), and finally water. After being dried (Na_2SO_4), the solution was distilled, giving: (*a*) glycide *o*-tolyl ether, b. p. 78—80°/0·2 mm. (10·2 g.) (Found: C, 72·6; H, 7·4. Calc. for $C_{10}H_{12}O_2$: C, 73·1; H, 7·3%); (*b*) 1-chloro-3-*o*-tolyloxypropan-2-ol, b. p. 95—110°/0·1 mm. (3·4 g.); glycide β-naphthyl ether, b. p. 120—130°/0·1 mm. (20·5 g.); there was a small residue (2 g.).

The ether-insoluble portion was added to water (300 c.c.). The resulting suspension was extracted by means of ether and the clear aqueous solution was diluted to 500 c.c. A portion of the solution (50 c.c.) was mixed with aqueous sodium picrate; an oily precipitate formed which soon solidified. Crystallisation from methanol containing a small proportion of dioxan gave 2·7 g. of *2′-hydroxy-3′-β-naphthoxypropylpyridinium picrate*, m. p. 154—155° (Found: N, 10·9. $C_{24}H_{20}O_9N_4$ requires N, 11·0%).

(iv) Table III summarises the results of a number of experiments in which various epoxide–chlorohydrin pairs were heated together in the presence of pyridine for the periods and at the temperatures stated. The yields of the quaternary chlorides isolated (*d*) are given. In the two experiments involving glycide β-naphthyl ether the quaternary salts were isolated as picrates.

TABLE III.

(*a*.)	(*b*.)	(*c*.)				
C_5H_5N (mols.).	RO·CH_2·CH—CH_2, R =	R′O·CH_2·CH(OH)·CH_2Cl, R′ =	Mol. ratio *a* : *b* : *c*.	Temp.	Time (hrs.).	Yield of (*d*),* %.
0·1	*o*-C_6H_4Me	*o*-C_6H_4Me	1 : 1 : 1	60°	0·5	20
0·1	,,	,,	1 : ,, : ,,	,,	1·0	30
0·1	,,	,,	1 : 2 : 2	,,	1·5	65
0·1	,,	*p*-C_6H_4Cl	1 : 2 : 2	55	1·25	*ca.* 50
0·1	*m*-C_6H_4Me	*m*-C_6H_4Me	1 : 2 : 2	60	1·5	65
0·1	*p*-C_6H_4Me	*p*-C_6H_4Me	1 : 2 : 2	60	1·5	65
0·1	*p*-C_6H_4Cl	*p*-C_6H_4Cl	1 : 2 : 2	60	1·5	65
0·1	Ph	Ph	1 : 2 : 2	60	1·5	60
0·1	β-$C_{10}H_7$	β-$C_{10}H_7$	1 : 2 : 2	60	1·5	*ca.* 55
0·1	,,	*m*-C_6H_4Me	1 : 2 : 2	55	1·25	*ca.* 50
0·1	*p*-C_6H_4Cl	,,	1 : 2 : 2	60	1·25	55
0·05	H	H	1 : 1 : 4	30	1·0	*ca.* 25

* The quaternary chloride (*d*) = RO·CH_2·CH(OH)·CH_2·NC_5H_5)Cl, where R is the same as in col. (*b*).

(v) Following are the properties of the other quaternary salts referred to in Table III: *2′-Hydroxy-3′-m-tolyloxypropylpyridinium chloride*, needles, m. p. 127—128° (Found: C, 64·1; H, 6·5; N, 4·9. $C_{15}H_{16}O_2NCl$ requires C, 64·4; H, 6·4; N, 5·0%); the *picrate* crystallised from methanol in yellow needles, m. p. 136—137° (Found: N, 11·7. $C_{21}H_{18}O_9N_4$ requires N, 11·9%). *2′-Hydroxy-3′-p-tolyloxypropylpyridinium chloride*, needles, m. p. 158—159° (Found: C, 64·5; H, 6·4; N, 4·9%); the *picrate* crystallised from methanol in yellow rhombs, m. p. 135° (Found: N, 11·8%). *3′-p-Chlorophenoxy-2′-hydroxypropylpyridinium chloride*, lustrous needles, m. p. 176—177° (Found: C, 55·8; H, 5·2; N, 4·5. $C_{14}H_{15}O_2NCl_2$ requires C, 56·0; H, 5·0; N, 4·7%); the *picrate* separated from methanol–dioxan in lustrous yellow needles, m. p. 164° (Found: N, 11·3. $C_{20}H_{17}O_9N_4Cl$ requires N, 11·4%).

In the following instance the crude chloride was not crystallised. It was dissolved in water, and sodium picrate added to precipitate the quaternary picrate. *2′-Hydroxy-3′-m-methoxyphenoxypropylpyridinium picrate* crystallised from methanol in fine yellow needles, m. p. 137—138° (Found: N, 11·6%).

Reaction of Pyridine with Glycide β-Naphthyl Ether.—A mixture of pyridine (7·9 g.) and glycide β-naphthyl ether (40 g.) was heated at 60° for an hour. The dark red-brown viscous product was added to dry ether (250 c.c.) with good stirring. The supernatant solution was decanted from the undissolved gum and this was stirred thoroughly with two additional 150-c.c. portions of dry ether. The residue weighed 13 g. It was used in the following experiments:

(*a*) 4 G. of the gum were shaken with distilled water (150 c.c.); an emulsion formed and this was extracted twice by means of ether. The clear aqueous solution which resulted was mixed with an excess of aqueous picric acid or, better, sodium picrate. An immediate precipitate formed; it was a gum initially, but it gradually solidified. Crystallisation from methanol containing a small proportion of dioxan afforded glistening, feathery, yellow plates (2·2 g.), m. p. 153—154°, not depressed on admixture with 2′-hydroxy-3′-β-naphthoxypropylpyridinium picrate (Found: N, 10·8%) (above). (*b*) A similar 4-g. portion of the gum was treated as in (*a*) except that 2N-hydrochloric acid (150 c.c.) was used instead

of picric acid. To the resulting solution was added an excess of aqueous picric acid. A picrate, m. p. 153—154° (2 g.), identical with that prepared in (*a*) separated. (*c*) 2 G. of the gum were mixed with 2N-sodium hydroxide solution (75 c.c.). The emulsion which formed gradually settled; after 12 hours the red-brown supernatant solution was decanted, neutralised with dilute acetic acid, and mixed with aqueous sodium picrate. A gum separated, followed by a solid. Crystallisation of the solid from methanol gave 0·1 g. of a product m. p. 153—154°, identical with the picrate prepared in (*a*).

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360. 2 : 3-*Bis*-p-*dimethylaminophenylbutane*-2 : 3-*diol*.

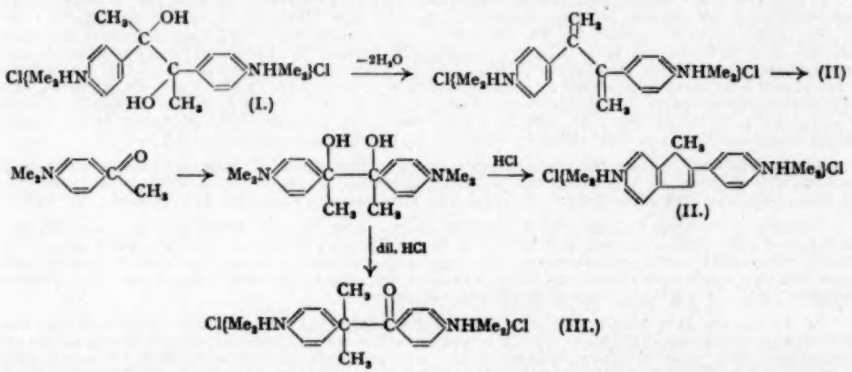
By MILTON J. ALLEN.

The pinacol from *p*-dimethylaminoacetophenone was prepared by electrolytic reduction, in two forms. Treatment of either form with very dilute hydrochloric acid yielded the pinacone 1 : 2-di-*p*-dimethylaminophenyl-2-methylpropan-1-one dihydrochloride, and a more concentrated acid gave 6-dimethylamino-2-*p*-dimethylaminophenyl-3-methylindene.

RECENTLY Allen and Corwin (*J. Amer. Chem. Soc.*, 1950, **72**, 117) described the formation of 6-amino-2-*p*-aminophenyl-3-methylindene from 2 : 3-bis-*p*-aminophenylbutane-2 : 3-diol and of 6-amino-2-*p*-aminophenyl-3-ethyl-1-methylindene from 3 : 4-di-*p*-aminophenylhexane-3 : 4-diol. Indene formation occurred when the diols were treated with an excess of hydrochloric acid. In addition, the respective pinacones, 1 : 2-di-*p*-aminophenyl-2-methylpropan-1-one and 1 : 2-di-*p*-aminophenyl-2-ethylbutan-1-one were also isolated from the reaction mixtures. Attempts to obtain indenes without pinacones by varying the concentration of acid proved unsuccessful.

In the preparation of 2 : 3-bis-*p*-dimethylaminophenylbutane-2 : 3-diol by electrolytic reduction at constant reference potential with the apparatus and cells previously described (Allen, *Analyt. Chem.*, 1950, **22**, 804; *J. Org. Chem.*, 1950, **15**, 435), an acidic medium and a reference potential of −1·5 volts gave the high-melting form of the pinacol, whereas a basic medium and a reference potential of −2·2 volts gave a low-melting form.

Treatment of either of the two stereoisomeric pinacols (I) with a quantity of dilute hydrochloric acid comparable to that which converted the pinacols of *p*-aminoacetophenone and *p*-aminopropiophenone into the respective pinacones exclusively gave in this case only the



indene (II) and in very good yield. A much smaller quantity of acid was sufficient to cause the pinacol to undergo a pinacol–pinacone rearrangement to the ketone (III). Apparently

dimethylamino-groups exert a greater influence on ring closure than do amino-groups themselves.

Application of the mechanism previously described by Allen and Corwin serves as a strict structural analogy for the formation of (II) from (I).

The ketone formed is 1 : 2-bis-*p*-dimethylaminophenyl-2-methylpropan-1-one (as III), by analogy with the ketones obtained by pinacol–pinacolone rearrangement of the aforementioned amino-pinacols, and this is confirmed by a comparison of its infra-red spectum with that of 1 : 2-di-*p*-aminophenyl-2-methylpropan-1-one. This shift of the methyl group is consistent with previous work on symmetrical pinacols (Bachmann and Sternberger, *J. Amer. Chem. Soc.*, 1934, **56**, 170; Price and Mueller, *ibid.*, 1944, **66**, 634) in which it was demonstrated that the strongest electron-donating group migrates : in this case the methyl group is the strongest electron-donating group owing to the deactivating influence of the dimethylammonium substituents on the benzene ring.

Experimental.

M. p.s were taken on a Kofler hot stage and are corrected.

2 : 3-*Bis*-p-*dimethylaminophenylbutane*-2 : 3-*diol*.—The catholyte consisted of *p*-dimethylaminoacetophenone (8 g.) in concentrated hydrochloric acid (7·2 ml.) and distilled water (42·8 ml.). A solution of concentrated hydrochloric acid (2·8 ml.) and distilled water (17·1 ml.) served as the anolyte. At a reference potential of −1·5 v. and 27° the initial current was 4·3 amps. After 22 minutes of electrolysis a current plateau of 2·5 amps. was reached, accompanied by the evolution of hydrogen at the cathode. The catholyte was filtered, made basic to litmus with dilute aqueous sodium hydroxide, and chilled. The precipitate was filtered off, washed with water, triturated with hot 70% acetone, and refrigerated overnight. The *butanediol* was filtered off and dried (6·8 g.). Recrystallization from acetone yielded white prisms, m. p. 186·1—187° (Found : C, 73·25; H, 8·8. $C_{20}H_{28}O_2N_2$ requires C, 73·1; H, 8·6%).

The lower-melting form of the pinacol was obtained in the following manner : *p*-Dimethylaminoacetophenone (3 g.) was dissolved in warm ethanol (48 ml.). To this was added 10% aqueous potassium hydroxide (24 ml.). The anolyte consisted of 2 : 1 ethanol–10% aqueous potassium hydroxide. At a reference potential of −2·2 v. and 32° the initial current was 3·0 amps. After 12 minutes of electrolysis a current plateau of 1·1 amps. was reached. During the reduction a precipitate formed in the catholyte, increasing in quantity as the reduction progressed. The catholyte was diluted with water (24 ml.) and refrigerated overnight. The precipitate was filtered off and dried (2·3 g.). Recrystallization from 50% ethanol yielded a *form*, m. p. 163·3—164·3° (Found : C, 73·3; H, 8·6%).

6-*Dimethylamino*-2-p-*dimethylaminophenyl*-3-*methylindene*.—The pinacol (2 g.) was refluxed (1½ hours) with concentrated hydrochloric acid (7 ml.) and water (14 ml.). The solution was evaporated to dryness and the residue triturated with a small amount of absolute ethanol. The oily residue began to solidify and after addition of an equal quantity of ethyl acetate the mixture was refrigerated. The white solid was filtered off, washed with ethyl acetate–ethanol (7 : 3) and then ether, and dried (1·8 g.). The *indene* decomposed at 212—214°. Recrystallization from anhydrous *n*-propyl alcohol gave a white crystalline solid decomposing at 212—214° (Found : C, 65·95; H, 7·2; N, 7·4. $C_{20}H_{24}N_2Cl_2$ requires C, 65·75; H, 7·2; N, 7·7%). The mother-liquors from the crystallization yielded only unidentifiable tars.

The free *base* was prepared from the *dihydrochloride* by neutralization of an aqueous solution. The precipitate, on crystallization from absolute methanol, yielded light yellow rosettes, m. p. 112—113° (Found : C, 81·9; H, 8·5. $C_{20}H_{24}N_2$ requires C, 82·1; H, 8·3%).

2-*Di*-p-*dimethylaminophenyl*-2-*methylpropan*-1-*one Dihydrochloride*.—A sample of the pinacol (1·85 g.) was dissolved in concentrated hydrochloric acid (1·38 ml.) and water (27·75 ml.) and refluxed for 1 hour. The solution was evaporated to dryness and the solid residue triturated with absolute ethanol (5 ml.) to which was added ethyl acetate (5 ml.). The chilled solution was filtered and the precipitate washed with ether. Recrystallization from ethanol–ether yielded the *ketone* (1·65 g.), m. p. 118—119° (Found : C, 62·9; H, 7·6. $C_{20}H_{26}ON_2Cl_2$ requires C, 62·7; H, 7·4%).

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361. *The Reactions of Unsaturated Compounds. Part IX.* The Oxidation of* as-*Dineopentylethylene by Chromic Oxide.*

By W. J. Hickinbottom and D. G. M. Wood.

Oxidation of *as*-di*neo*pentylethylene by chromic oxide in acetic anhydride yields 1 : 2-epoxy-1 : 1-di*neo*pentylethane. The significance of this observation is discussed.

It is shown below that oxidation of *as*-di*neo*pentylethylene (4 : 4-dimethyl-2-*neo*pentylpent-1-ene) (I) by chromium trioxide in acetic anhydride solution yields 1 : 2-epoxy-1 : 1-di*neo*pentylethane (II) as the main product; a small amount of di*neo*pentylacetic acid (III) is also formed. No other product could be isolated or identified.

Bartlett, Fraser, and Woodward's observations (*J. Amer. Chem. Soc.*, 1941, **63**, 496) that this epoxide is not hydrated to a glycol by dilute sulphuric acid have been confirmed and extended. It has not been possible to obtain the glycol from it even by prolonged boiling with aqueous alcohol; when it was sought to convert it into the chlorohydrin by the action of hydrogen chloride in ether (Swern *et al.*, *Ind. Eng. Chem. Anal.*, 1947, **19**, 414) there was no measurable uptake of hydrogen chloride; the epoxide did not react with sodiomalonic ester. Aqueous acids isomerise it to di*neo*pentylacetaldehyde, which is readily oxidised to di*neo*pentylacetic acid (III). This acid is also formed in good yield by oxidation of (I) or of (II) by chromic acid in aqueous sulphuric acid (Whitmore and Surmatis, *J. Amer. Chem. Soc.*, 1941, **63**, 2200; Bartlett, Fraser, and Woodward, *loc. cit.*).

$(CMe_3\cdot CH_2)_2C{:}CH_2$ (I.) $\quad$ $(CMe_3\cdot CH_2)_2C\!-\!CH_2$ (II.) $\quad$ $(CMe_3\cdot CH_2)_2CH\cdot CO_2H$ (III.)

It was suggested by Byers and Hickinbottom (*J.*, 1948, 1334) that the oxidation of an olefin by chromic acid in aqueous sulphuric acid depends on the initial formation of an epoxide, and that the course of the oxidation is determined by the behaviour of the epoxide in aqueous acid. The observations on the oxidation of di*neo*pentylethylene provide satisfactory support for this hypothesis, in that the almost quantitative isomerisation of the epoxide to di*neo*pentylacetaldehyde and its subsequent oxidation to di*neo*pentylacetic acid is in striking qualitative agreement with the formation of di*neo*pentylacetic acid as the main product of oxidation of the olefin.

If the isomerisation of the epoxide is accompanied by the formation of the glycol, it is postulated that the oxidation of the olefin by chromic acid in aqueous sulphuric will lead to a mixture of products derived from the oxidative fission of the glycol and from the oxidation of the isomerisation product. These deductions are borne out by the behaviour of 2 : 4 : 4-trimethylpent-1-ene (IV), which yields 2 : 4 : 4-trimethylpentanoic acid (V) † as well as methyl *neo*pentyl ketone (VI). The formation of 2 : 2 : 3 : 3-tetramethylbutanoic acid (VIII), acetone, and trimethylacetaldehyde from 2 : 4 : 4-trimethylpent-2-ene (VII) is a further example supported by observations on the corresponding epoxide (Byers and Hickinbottom, *loc. cit.*; Whitmore *et al.*, *J. Amer. Chem. Soc.*, 1941, **63**, 2028).

$CMe_3\cdot CH_2\cdot CMe{:}CH_2$ (IV.) $\quad$ $CMe_3\cdot CH_2\cdot CHMe\cdot CO_2H$ (V.) $\quad$ $CMe_3\cdot CH_2\cdot COMe$ (VI.)

$CMe_3\cdot CH{:}CMe_2$ (VII.) $\quad$ $CMe_3\cdot CMe_2\cdot CO_2H$ (VIII.)

The formation of epoxides from olefins by the action of chromium trioxide has also been realised in acetic acid solution. Tetraphenylethylene and some of its halogen and nitro-derivatives (Behr, *Ber.*, 1872, **5**, 277; Norris, Thomas, and Brown, *Ber.*, 1910, **43**, 2954; Biltz, *Annalen*, 1897, **296**, 23; Bockemüller and Jansen, *ibid.*, 1939, **542**, 166), some 8 : 14- and 8 : 9-unsaturated sterols (Staveley and Bollenback, *J. Amer. Chem. Soc.*, 1943, **65**, 1285, 1290, 1600; Wintersteiner and Moore, *ibid.*, p. 1513), and some αβ-unsaturated steroid alcohols (Petrow *et al.*, *J.*, 1939, 998; 1940, 60) are reported to form epoxides when oxidised in acetic acid by chromic oxide. It seems a reasonable inference that the initial phase of the oxidation by chromium trioxide is the same whether it be in acetic acid or in acetic anhydride. The

* Part VIII, *J.*, 1948, 1334. † Geneva notation, CO_2H = 1, is used for these acids.

comparative stability of these epoxides no doubt permits of their survival during the reaction. Less stable oxides cannot survive in these conditions, yet it has been possible to obtain unambiguous evidence of their participation in some oxidations (Hickinbottom and Wood, unpublished; Fieser and Fieser, " Natural Products related to Phenanthrene," 1949, p. 231).

In the oxidation of olefins by chromic acid in aqueous sulphuric acid it is improbable if epoxides are formed that they can survive. Evidence of their participation in the reaction must rely on their isomerisation to aldehydes and ketones Experimental evidence of this nature has already been surveyed in the earlier part of this discussion.

It has sometimes been suggested that the oxidation of the olefinic double bond by chromic acid occurs through the initial formation of a glycol (compare Farmer and Pitkethly, *J.*, 1938, 287). Whatever may be the course of the reaction in special circumstances, it is unlikely that oxidation in general can occur in this way; it is known that the oxidative fission of 1 : 2-glycols by chromic acid occurs very easily (Byers and Hickinbottom, *loc. cit.*; cf. also Slack and Waters, *J.*, 1949, 594), and more rapidly than the glycol can isomerise in aqueous sulphuric acid to yield products which are characteristic of isomeric change in the oxidation.

Experimental.

(Analyses by Drs. Weiler and Strauss.)

Di*neo*pentylethylene(4 : 4-dimethyl-2-*neo*pentylpent-1-ene) was prepared from redistilled technical tri*iso*butylene by Bartlett, Fraser, and Woodward's method (*J. Amer. Chem. Soc.*, 1941, **63**, 495) with the modification that the amount of potassium permanganate was increased to 1200 g. for the oxidation of 168 g. of tri*iso*butylene. One sample of tri*iso*butylene with a low content of di*neo*pentylethylene required two such oxidations before a pure sample of the olefin was obtained.

Di*neo*pentylethylene prepared in this way from two different samples of tri*iso*butylene had b. p. 179°/760 mm., 112—113°/100 mm., 75°/32 mm. (all uncorr.); n_D^{20} 1·4283—1·4289. It was distilled over sodium before use.

1 : 2-Epoxy-1 : 1-di*neo*pentylethane(2 : 2'-di*neo*pentyloxiran) (II) was prepared from di*neo*pentylethylene by the action of perbenzoic acid in chloroform. Its constants, b. p. 90°/20 mm., n_D^{20} 1·4331, agree with those recorded by Bartlett, Fraser, and Woodward (*loc. cit.*), *viz.*, 85—88°/15 mm., n_D^{20} 1·4330.

The facile isomerisation of the epoxide to di*neo*pentylacetaldehyde (3 : 3-dimethyl-2-*neo*pentylbutanal) under the influence of dilute acids was confirmed. It readily yields *dineopentylacetaldehyde* 2 : 4-*dinitrophenylhydrazone*, orange needles, m. p. 185° (Found : C, 59·7; H, 7·3; N, 15·1. $C_{18}H_{28}O_4N_4$ requires C, 59·3; H, 7·7; N, 15·4%) when mixed with an alcoholic solution of 2 : 4-dinitrophenylhydrazine containing some concentrated sulphuric acid.

In other respects the epoxide is relatively stable. It is substantially unchanged when refluxed with sodium for 10 minutes; it could not be induced to react with sodiomalonic ester. No glycol could be obtained by refluxing it with aqueous alcohol for 178 hours followed by keeping the product at room temperature for six weeks. The products from 3·1 g. of epoxide were di*neo*pentylacetic acid (1·0 g.) and a neutral fraction (1·1 g.), b. p. 94—110°/25 mm., which gradually solidified in the air with the formation of di*neo*pentylacetic acid; a residue (0·1 g.) could not be further identified. Attempts to estimate the epoxide by measuring the uptake of hydrogen chloride in ethereal solution gave no result.

Reduction of the epoxide in boiling ethereal solution by lithium aluminium hydride gave a mixture, b. p. 84—103°/18 mm., n_D^{20} 1·4359—1·4428, from which methyldi*neo*pentylcarbinol was isolated as its 3 : 5-*dinitrobenzoate*, m. p. 138°, by chromatographing the esters of the crude alcohol (Found : C, 60·0; H, 7·25; N, 7·0. $C_{19}H_{28}O_6N_2$ requires C, 60·0; H, 7·4; N, 7·4%). The 3 : 5-dinitrobenzoate of 2 : 2-di-*neo*pentylethanol was also isolated, m. p. and mixed m. p. 101°. The proportion of these two alcohols was not determined but it appears that methyldi*neo*pentylcarbinol is the more abundant.

For the purposes of comparison, 2 : 2-di*neo*pentylethanol was prepared by reduction of di*neo*pentylacetic acid by lithium aluminium hydride in boiling ether.

Oxidation of Dineopentylethylene by Chromium Trioxide in Acetic Anhydride.—A number of these oxidations were carried out on the olefin which had been refluxed over sodium and redistilled immediately before use. The results in all oxidations were substantially the same. The following describes one such oxidation. A solution of chromium trioxide (14 g.) in freshly distilled acetic anhydride (80 ml.) was added during one hour to an efficiently stirred solution of di*neo*pentylethylene (n_D^{20} 1·4290; 40 g.) in acetic anhydride (38 ml.) cooled in ice–salt. When addition was complete, the solution was kept at below 0° and stirred continuously for 2 hours. Water (350 ml.) was then run in slowly, and the stirring and cooling continued till the hydrolysis of the anhydride was substantially complete. The upper layer was then separated and combined with two ether extracts of the aqueous layer. After being washed repeatedly with concentrated sodium carbonate solution and dried (K_2CO_3), it was distilled : fraction (*a*), b. p. 76—84°/34 mm., $n_D^{20\cdot1}$ 1·4285—1·4288, consisted essentially of unchanged olefin; the main product of the oxidation (*b*) was collected at 95—100°/27 mm. (11 g.); there was also a small residue of di*neo*pentylacetic acid (ββ-dimethyl-α-*neo*pentylbutyric acid).

From (*b*) a substantially pure product was isolated by further fractionation; b. p. 95—96°/25 mm., n_D^{20} 1·4326—1·4329, d^{20} 0·8374. These constants agree well with those of 1 : 2-epoxy-1 : 1-di*neo*pentylethane (b. p. 90°/20 mm., 100°/32 mm.; n_D^{20} 1·4331; d^{20} 0·8367). A portion (2·2 g.) gave 2·0 g. unchanged after reaction with Girard T reagent. This material was unaltered after being heated with sodium

(0·2 g.) for 15 minutes; n_D^{20} 1·4340 [Found: C, 78·4; H, 13·0%; *M* (Rast), 179. Calc.: C, 78·2; H, 13·1%; *M*, 184]. The absence of any considerable amount of di*neo*pentylacetaldehyde was shown not only by its indifference to Girard reagent but also by its stability on exposure to air for several days. In contact with a little dilute sulphuric acid, it gradually solidifies to di*neo*pentylacetic acid; with an alcoholic sulphuric acid solution of 2 : 4-dinitrophenylhydrazine, the 2 : 4-dinitrophenylhydrazone of di*neo*pentylacetaldehyde was formed, m. p. and mixed m. p. 185°. Reduction in boiling ether by lithium aluminium hydride yielded methyldi*neo*pentylcarbinol, characterised by its 3 : 5-dinitrobenzoate, m. p. and mixed m. p. 138°.

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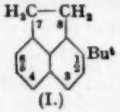
362. *Acenaphthene Series. Part V.* Preparation and Orientation of the Three Nuclear-substituted Mono-*tert.*-butylacenaphthenes. Isolation of Pure* 1-tert.*-Butylnaphthalene.*

By ERIC ILLINGWORTH and ARNOLD T. PETERS.

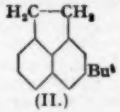
Although acenaphthene with *tert.*-butyl chloride and aluminium chloride in carbon disulphide gives 2-*tert.*-butyl- and 2 : 5-di-*tert.*-butyl-acenaphthene, use of anhydrous ferric chloride as catalyst yields surprisingly 1- and 3-*tert.*-butyl- and 1 : 6-di-*tert.*-butyl-acenaphthene. These products have been orientated by synthesis or degradation, and many new derivatives, including thioindigoid vat dyes, have been prepared.

3-*tert.*-Butylacenaphthene was converted into 4-*tert.*-butylnaphthalic anhydride and thence into 1-*tert.*-butylnaphthalene. This is the first record of the preparation of pure 1-*tert.*-butylnaphthalene, which was also synthesised from 1-tetralone by a Grignard reaction.

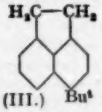
2-*tert.*-BUTYL- (II) AND 2 : 5-DI-*tert.*-BUTYLACENAPHTHENE, prepared from acenaphthene by the Friedel–Crafts reaction with aluminium chloride (Peters, *J.*, 1942, 562), were orientated by Nürsten and Peters (*J.*, 1950, 729). When ferric chloride was used as catalyst, 1- (I) and 3-*tert.*-butylacenaphthene (III) were formed, the relative proportions depending on the temperature of reaction; the approximate proportions of the 1- and the 3-isomer in the total mono-*tert.*-butyl fractions formed were 45 : 55 in boiling carbon disulphide, and 83 : 17 in the same solvent at 10—15°. Some 1 : 6-di-*tert.*-butylacenaphthene was also isolated, but was difficult to obtain crystalline owing to the presence of a yellow resin.



(I.)



(II.)



(III.)

Orientation of 3-tert.*-Butylacenaphthene* (III).—This compound, which gave a *s*-trinitrobenzene complex, was oxidised by sodium dichromate in boiling acetic acid to 4-*tert.*-butylnaphthalic anhydride, from which were prepared the corresponding imide, *N*-methyl- and *N*-hydroxyethyl-imide, and 3′-keto-6′(or 7′)-*tert.*-butyl-2′-azaperinaphthano(1′ : 2′-2 : 1)benziminazole,† by methods described in previous Parts of this series. The anhydride was then converted into a *tert.*-butylnaphthalene by distillation with soda-lime, or better, by conversion through the mercuri-derivative into a mixture of 4- and 5-*tert.*-butyl-1-naphthoic acids, followed by decarboxylation by copper bronze in boiling quinoline.

* Part IV, *J.*, 1950, 2389.

† In *J.*, 1950, 729 this system was named 8′-azaphenalino(7′ : 8′-2 : 1)benziminazole. For details of the nomenclature change see *J.*, 1950, 3701.

The derived 1-*tert.*-butylnaphthalene gave a picrate which differed from that obtained from 2-*tert.*-butylnaphthalene prepared either by direct *tert.*-butylation of naphthalene or by unambiguous synthesis (cf. Bromby *et al.*, *J.*, 1943, 144). Attempted conversion of 1-*tert.*-butylnaphthalene into 1-naphthoic acid by dilute nitric acid at 180° yielded only the solid 4-nitro-derivative which was also obtained by nitric and 80% sulphuric acid at 50°. In contrast, the nitro-compound prepared from 2-*tert.*-butylnaphthalene by either of these methods could not be obtained crystalline.

Dr. N. G. Bromby (Thesis, Leeds Univ., 1941) attempted the synthesis of 1-*tert.*-butylnaphthalene by interaction of *tert.*-butylmagnesium chloride and 1-tetralone, followed by dehydration of the resulting carbinol to 1-*tert.*-butyl-3 : 4-dihydronaphthalene, which was then dehydrogenated with sulphur. The reaction was abnormal, probably owing to steric hindrance and the reducing action of *tert.*-butylmagnesium chloride. It gave naphthalene and 2-*tert.*-butylnaphthalene, with a small amount of an oil which afforded a picrate, m. p. 101·5—102·5°, which analysed correctly for a *tert.*-butylnaphthalene picrate; the m. p. (100—101·5°) of 2-*tert.*-butylnaphthalene picrate was depressed to 77—95°. Moreover, the 1-*tert.*-butylnaphthalene obtained by the present authors by degradation of 3-*tert.*-butylacenaphthene gave a picrate, m. p. 101·5—102·5°, not depressed on admixture with the synthetic product prepared from 1-tetralone. Thus the orientation of 3-*tert.*-butylacenaphthene is established.

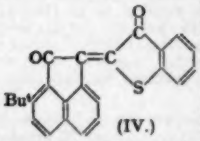
Tsukervanik and Terentieva (*J. Gen. Chem. U.S.S.R.*, 1937, **7**, 637) record that 1-alkylnaphthalenes are isomerised to 2-alkylnaphthalenes merely by heating them, but Cullinane and Chard (*Nature*, 1948, **161**, 690), who converted 1- into 2-methylnaphthalene, used alumina as catalyst at 450°, whilst Mayer and Schiffner (*Ber.*, 1934, **67**, 67) employed silica gel in a porcelain tube at 350° for the conversion of 1- into 2-alkylnaphthalenes. On refluxing 1-*tert.*-butylnaphthalene or 3-*tert.*-butylacenaphthene for 8 hours, however, we found no isomerisation; in the presence of a suitable catalyst, some migration of *tert.*-butyl occurs, and such reactions are under investigation.

For an analogous *tert.*-butylation of toluene, Buu-Hoï and Cagniant (*Bull. Soc. chim.*, 1942, **9**, 887) state that the use of aluminium chloride affords mainly *m*-*tert.*-butyltoluene, whilst ferric chloride gives mainly the *p*-isomer (cf. Baur, *Ber.*, 1891, **24**, 2833; Bialobrzeski, *Ber.*, 1897, **30**, 1773).

Controlled oxidation of 3-*tert.*-butylacenaphthene (III) with sodium dichromate and acetic acid gave 3-*tert.*-butylacenaphthenequinone, which condensed with 3-hydroxythionaphthen and its 6-ethoxy-derivative, to yield red indigoid vat dyes.

3-*tert.*-Butylacenaphthene readily afforded a crystalline monobromo-derivative with 1 or 2 mols. of bromine, whereas monobromo-2-*tert.*-butylacenaphthene could not be obtained pure and the dibromo-compound was readily isolated (*loc. cit.*).

Orientation of 1-tert.-*Butylacenaphthene.*—Oxidation of this hydrocarbon, which proceeds less readily than that of the 2- or the 3-isomeride, gave 2-*tert.*-butylnaphthalic anhydride, which was converted by soda-lime distillation into 2-*tert.*-butylnaphthalene, identical with a specimen prepared by unambiguous synthesis. Moreover, derivatives of 2-*tert.*-butylnaphthalic anhydride were shown to be isomeric with, but different from, the analogues prepared from 3- or 4-*tert.*-butylnaphthalic anhydride, but owing to the position of the *tert.*-butyl group they were obtained less readily. Further, 1-*tert.*-butylacenaphthenone, prepared by a modification of Buu-Hoï and Cagniant's method (*Rev. sci.*, 1942, **80**, 176 *), was oxidised to 2-*tert.*-butylnaphthalic anhydride, identical with that from 1-*tert.*-butylacenaphthene. Controlled oxidation of the latter afforded 1-*tert.*-butylacenaphthenequinone which condensed with 3-hydroxythionaphthen to yield an apparently homogeneous red dye, 1′-*tert.*-butyl-2 : 7′-thionaphthenacenaphthenylindigo (IV); it is unlikely that condensation occurs at the 8-position *ortho* to the *tert.*-butyl group.



(IV.)

Orientation of 1 : 6-*Di*-tert.-*butylacenaphthene.*—This hydrocarbon was much more resistant to oxidation than any of the three mono-*tert.*-butylacenaphthenes or 2 : 5-di-*tert.*-butylacenaphthene; even after 24 hours' boiling with sodium dichromate and acetic acid a mixture of di-*tert.*-butyl-acenaphthenequinone and -naphthalic anhydride resulted. Subsequent distillation with soda-lime afforded 2 : 7-di-*tert.*-butylnaphthalene identical with that prepared by direct di-*tert.*-butylation of naphthalene or by soda-lime distillation of 3 : 6-di-*tert.*-butylnaphthalic anhydride (cf. Nürsten and Peters, *loc. cit.*). This proves that the di-*tert.*-butylacenaphthene, formed from acenaphthene as above, is the 1 : 6-derivative, and this is supported

* Acknowledgment is given to Dr. Buu-Hoï, who kindly sent to us reprints of his papers in *Rev. sci.*

by the relative stability of the substance to oxidising agents and by the inability of the derived 1 : 6-di-*tert.*-butylacenaphthenequinone to give a thioindigoid vat dye.

Melting points are compared in the attached Table. Although those of 2- and 4-*tert.*-butylnaphthalic anhydride and their analogous derivatives are almost identical, depressions in m. p. of 25—30° are observed in each case.

Position of Bu^t group :	1	2	3
tert.-Butylacenaphthene	65—66°	88—88·5	101·5—102°
Do., picrate	93—95	121—123	Not formed
Do., trinitrobenzene complex	118—119	149—150	87—88
tert.-Butylacenaphthenequinone	152—154·5	156—159	138—139
tert.-Butyl-2 : 7′-thionaphthacenaphthenylindigo	260—262	300—301	186—188
Position of Bu^t group :	2	3	4
tert.-Butylnaphthalic anhydride	163—164°	204—205°	165—166°
tert.-Butylnaphthalimide	201—202	256	208·5—210·5
tert.-Butyl-*N*-methylnaphthalimide	132—133	173	132—133
tert.-Butylnaphthalene, by degradation	2-; picrate, 100—101·5°	2-; picrate, 100—101·5°	1-; picrate, 101·5—102·5°

The migration of *tert.*-butyl groups in this series of compounds, by the action of catalysts, is being investigated. It is noteworthy that 2 : 5-di-*tert.*-butylacenaphthene is an excellent insulating material of convenient melting point (162°), *e.g.*, for thermo-couple joints.

Experimental.

Micro-analyses were carried out by Drs. Weiler and Strauss, of Oxford.

3-tert.-*Butylacenaphthene* (III).—Anhydrous ferric chloride (66 g., 0·2 mol.) was added to a stirred solution of acenaphthene (308 g., 1 mol.) in carbon disulphide (800 c.c.) at 40°. *tert.*-Butyl chloride (240 c.c., 1·1 mols.) was then introduced during 30 minutes, with vigorous stirring; an efficient condensing system is essential, as the hydrogen chloride liberated tends to carry away *tert.*-butyl chloride. After 4 hours' refluxing the mixture was filtered (charcoal), the carbon disulphide distilled off, and the reddish-brown oil fractionated (24″ column; steam-jacketed condenser to eliminate loss by sublimation and to prevent blockage), to give unchanged acenaphthene (80 g.), b. p. 270°/760 mm., a mixture (11 g.), b. p. 270—319°, and *tert.*-butylacenaphthenes (125 g.), b. p. 319—321°; the resinous residue, b. p. >360°, was distilled at 15 mm. and yielded 102 g. of a pale yellow glass, b. p. 190—200°. The main fraction (125 g.) solidified and was crystallised repeatedly from absolute alcohol to give large, colourless, prismatic needles, m. p. 101·5—102°, of 3-tert.-*butylacenaphthene* (46 g.) (Found: C, 91·5; H, 8·3. $C_{16}H_{18}$ requires C, 91·4; H, 8·6%). On admixture with the 2- (m. p. 88—88·5°) or 1-isomer (m. p. 65—66°), the m. p. was depressed to 58° or 50°, respectively.

From the mother-liquors, a little pure 1-*tert.*-butylacenaphthene (2 g.) was isolated, and a mixture (A) (56 g.), m. p. 48—52° (Found: C, 91·1; H, 8·7%), of isomers, which could not be purified by fractional crystallisation. 3-*tert.*-Butylacenaphthene did not give a picrate, but in absolute alcohol afforded a *s-trinitrobenzene* complex, which crystallised from the same solvent in deep orange needles, m. p. 87—88° (Found: C, 62·7; H, 5·3; N, 9·8. $C_{16}H_{18}.C_6H_3O_6N_3$ requires C, 62·4; H, 5·0; N, 9·9%).

The above pale yellow glass (102 g.) was crystallised several times from acetic acid and then alcohol, to yield colourless, prismatic needles, m. p. 135—136·5°, b. p. 358—360°/758 mm., of 1 : 6-*di*-tert.-*butylacenaphthene* (60 g.) (Found: C, 90·4; H, 9·8. $C_{20}H_{26}$ requires C, 90·2; H, 9·8%). On admixture with 2 : 5-di-*tert.*-butylacenaphthene (m. p. 162—163°), the m. p. was depressed to 112°. In absolute alcohol, it gave a *picrate*, which crystallised from absolute alcohol in scarlet needles, m. p. 169—170° (Found: C, 63·2; H, 5·9; N, 8·3. $C_{20}H_{26}.C_6H_3O_7N_3$ requires C, 63·0; H, 5·9; N, 8·5%), and a *s-trinitrobenzene* complex, silky orange needles (from absolute alcohol), m. p. 194—195·5° (Found: C, 64·9; H, 5·9; N, 8·6. $C_{20}H_{26}.C_6H_3O_6N_3$ requires C, 65·1; H, 5·85; N, 8·8%). On admixture with 2 : 5-di-*tert.*-butylacenaphthene picrate, m. p. 165—165·5°, the m. p. of the 1 : 6-isomer was depressed to 135—140°.

x-*Bromo*-3-tert.-*butylacenaphthene*.—Bromine (1·3 c.c., 1·1 mols.) in chloroform (50 c.c.) was added to a solution of 3-*tert.*-butylacenaphthene (5 g., 1 mol.) in the same solvent (50 c.c.) during 20 minutes, at room temperature. Decolorisation was rapid, and after 1 hour at room temperature alcohol (100 c.c.) was added and the mixture concentrated to 100 c.c., crystallisation then beginning. The *bromo*-derivative crystallised from alcohol–chloroform in colourless needles, m. p. 178—179° (3·1 g., 57%) (Found: C, 66·3; H, 5·7; Br, 27·5. $C_{16}H_{17}Br$ requires C, 66·4; H, 5·9; Br, 27·7%). This bromination differs from that of 2-*tert.*-butylacenaphthene in that the use of 2 mols. of bromine in the above reaction affords solely the same monobromo-derivative.

3-tert.-*Butylacenaphthenequinone*.—Powdered sodium dichromate (45 g.) was added, all at once, with vigorous stirring, to a solution of 3-*tert.*-butylacenaphthene (15 g.) in acetic acid (400 c.c.) at 95°. After 6 minutes, when the vigorous reaction had subsided, the mixture was added to ice-water (600 g.) and set aside for 4 hours. The solid was collected, washed with water, and repeatedly extracted with 5% aqueous sodium carbonate at 80° to remove 4-*tert.*-butylnaphthalic anhydride (2 g., 12%). The insoluble residue was then extracted with sodium metabisulphite (50 g.) in boiling water (500 c.c.), and the extract acidified with hydrochloric acid, and boiled; on cooling, the resulting precipitate was

collected, washed with boiling 5% aqueous sodium carbonate, and crystallised from alcohol in orange-yellow needles, m. p. 138—139°, of 3-tert.-*butylacenaphthenequinone* (3·5 g., 20% of pure quinone) (Found: C, 80·5; H, 6·0. $C_{16}H_{14}O_2$ requires C, 80·7; H, 5·9%).

3′- + 4′-tert.-*Butyl*-2 : 7′-*thionaphthenacenaphthenylindigo*.—Freshly prepared 3-hydroxythionaphthen in acetic–hydrochloric acid (5 : 1) was added to a hot solution of 3-*tert.*-butylacenaphthenequinone in acetic acid; a scarlet colour developed immediately and, after 2 minutes' boiling and addition of a little water and cooling, the red precipitate was collected and crystallised several times from acetic acid in deep red prisms, m. p. 186—188°, of the thioindigoid vat *dye* (Found: C, 77·7; H, 4·9; S, 8·4. $C_{32}H_{18}O_2S$ requires C, 77·8; H, 4·9; S, 8·65%). It dissolves in cold concentrated sulphuric acid with a green colour, becoming pink on dilution. No separation could be effected by fractional crystallisation or chromatography, but it is probable that this relatively low-melting dye, which is more soluble in organic solvents than the 1′- or 2′-isomeride, is a mixture of isomers.

3′- + 4′-tert.-*Butyl*-6-*ethoxy*-2 : 7′-*thionaphthenacenaphthenylindigo*.—In similar manner, 6-ethoxy-3-hydroxythionaphthen gave the *dye* in red needles, m. p. 165—167° (shrinks from 163°) (Found: C, 75·4; H, 5·3. $C_{34}H_{22}O_3S$ requires C, 75·4; H, 5·6%), soluble in sulphuric acid with a Bordeaux colour, becoming pink on dilution.

4-tert.-*Butylnaphthalic Anhydride*.—Sodium dichromate (45 g.) was added to a solution of 3-*tert.*-butylacenaphthene (15 g.) in boiling acetic acid (400 c.c.), and the mixture refluxed for 5 hours. On addition of the mixture to ice-water (600 g.), the resulting precipitate was collected and extracted repeatedly with boiling 5% aqueous sodium carbonate. Acidification of the alkaline extracts gave the *anhydride*, which crystallised from alcohol in needles, m. p. 165—166° (16·5 g., 92%) (Found: C, 75·8; H, 5·3. $C_{16}H_{14}O_3$ requires C, 75·6; H, 5·5%).

4-tert.-*Butylnaphthalimide*, prepared in aqueous alcohol, crystallised from alcohol in prismatic needles, m. p. 208·5—210·5° (Found: C, 75·8; H, 5·6; N, 5·4. $C_{16}H_{15}O_2N$ requires C, 75·9; H, 5·9; N, 5·5%); the N-*methylimide* crystallised from alcohol in prismatic needles, m. p. 132—133° (Found: C, 76·4; H, 6·1; N, 5·2. $C_{17}H_{17}O_2N$ requires C, 76·4; H, 6·3; N, 5·2%); and the N-2-*hydroxyethylimide* formed needles, m. p. 127—128° (Found: C, 72·8; H, 6·6; N, 4·3. $C_{18}H_{19}O_3N$ requires C, 72·7; H, 6·4; N, 4·7%). When the anhydride (1 mol.) and *o*-phenylenediamine (1·4 mols.) were boiled in acetic acid for 10 minutes and diluted with a little water, canary-yellow needles of 3′-*keto*-6′(+7′)-tert.-*butyl*-2′-*aza-perinaphthano*(1′ : 2′-2 : 1)*benziminazole* separated (Found: C, 81·1; H, 5·6; N, 8·6. $C_{22}H_{18}ON_2$ requires C, 81·0; H, 5·5; N, 8·6%). The m. p. rose progressively on crystallisation from 188—194° to 220—221°, probably owing to the presence of the 6′- and 7′-*tert.*-butyl isomers. In alcohol solution, there was a strong green fluorescence.

x-Bromo-3-*tert.*-butylacenaphthene (2 g.) was oxidised in the usual way to x-*bromo*-4-tert.-*butylnaphthalic anhydride* (2 g.; 87%), which crystallised from acetic acid in colourless prismatic needles, m. p. 236—237° (Found: C, 57·5; H, 4·1; Br, 24·0. $C_{16}H_{13}O_3Br$ requires C, 57·6; H, 3·9; Br, 24·1%).

4- + 5-tert.-*Butyl*-1-*naphthoic Acid* (method: Leuch *et al.*, *J. Amer. Chem. Soc.*, 1929, **51**, 1835).—4-*tert.*-Butylnaphthalic anhydride (10 g.) was dissolved in boiling water (500 c.c.) containing sodium hydroxide (6·3 g.) in a large flask (much frothing), and a solution of mercuric oxide (8·6 g.) in acetic acid (14 c.c.) and water (37 c.c.) was added. A precipitate was formed immediately, and the suspension, which was just acid to litmus, was refluxed for 98 hours, with intermittent stirring. The solid mercuri-derivative was collected and hydrolysed by refluxing with hydrochloric acid (100 c.c.) and water (200 c.c.) for 2 hours. The resulting light brown solid (7·4 g.) coagulated and was collected and crystallised from alcohol in almost colourless needles, m. p. 130—139°, probably of mixed *tert.*-butyl-1-naphthoic acids.

1-tert.-*Butylnaphthalene*.—(*a*) The mixed *tert.*-butyl-1-naphthoic acids were refluxed with quinoline (20 c.c.) and copper bronze (2·5 g.) for 15 minutes and the mixture was then added to an excess of dilute hydrochloric acid. Distillation with steam, followed by extraction of the distillate with ether, gave 1-tert.-*butylnaphthalene* as an almost colourless oil (5 g., 70% calc. on anhydride), b. p. 90—95°/0·8—1 mm. (Found: C, 91·3; H, 8·2. $C_{14}H_{14}$ requires C, 91·5; H, 8·5%). The derived *picrate* crystallised from absolute alcohol in needles, m. p. 101·5—102·5° (Found: C, 58·0; H, 4·5; N, 10·2. $C_{14}H_{14},C_6H_3O_7N_3$ requires C, 58·1; H, 4·6; N, 10·2%), which depressed the m. p. (100—101·5°) of 2-*tert.*-butylnaphthalene picrate to 80—95°.

(*b*) 4-*tert.*-Butylnaphthalic anhydride (4 g.) was thoroughly ground with soda-lime and the mixture was distilled; the distillate was distilled with steam and gave, as above, 1-*tert.*-butylnaphthalene (1·5 g., 52%), b. p. 100°/2 mm. The picrate (Found: C, 58·0; H, 4·6; N, 10·0%) was identical with that obtained by method (*a*).

Attempted oxidation of 1-*tert.*-butylnaphthalene (0·5 g.) by 5% aqueous nitric acid (14 or 18 c.c.) at 160—180° for 20 hours gave no alkali-soluble naphthoic acid, but yielded a thick yellow oil; dissolution in ether, removal of solvent, and treatment with alcohol gave pale yellow needles, m. p. 91—92·5° (in both cases) (Found: C, 73·7; H, 6·7; N, 6·1. $C_{14}H_{15}O_3N$ requires C, 73·3; H, 6·55; N, 6·1%), of 4-*nitro*-1-tert.-*butylnaphthalene*. Under similar conditions, 2-*tert.*-butylnaphthalene gave oils, from which no solid product was isolable.

1-*tert.*-Butylnaphthalene was refluxed for 8 hours, at b. p. 272°, but an examination of the resulting picrate showed that no conversion into the 2-isomer had occurred. Similarly, 2- and 3-*tert.*-butylacenaphthene were unchanged.

Synthesis of 1-tert.-*Butylnaphthalene*.—1-Tetralone (prep.: Martin and Fieser, *Org. Synth.*, 1935, **15**, 77) (51·1 g., 0·35 mol.) in dry ether (150 c.c.) was added during 20 minutes to a cold ethereal solution (520 c.c.) of *tert.*-butylmagnesium chloride, prepared from magnesium (61 g.) and *tert.*-butyl chloride (227 g.) in ether (1100 c.c.) (evaluated by titration by Gilman's method, *J. Amer. Chem. Soc.*, 1923, **45**,

150). The mixture was refluxed for 2 hours and kept overnight; a mixture of sulphuric acid (25 c.c.) and water (200 c.c.) was added and the resulting precipitate dissolved on shaking. The ethereal layer was collected, washed with water, and dried (Na_2SO_4); removal of ether gave a straw-coloured liquid (57 g.) of the carbinol. This was refluxed with acetic anhydride (300 c.c.) for 4 hours and set aside at room temperature overnight, and then hot water (300 c.c.) was added to decompose excess of acetic anhydride, and the solution neutralised with aqueous sodium carbonate. On ether-extraction, a dark oil (42 g.) resulted, which was distilled and fractionated at 8 mm. to give oils, b. p. 80—100° (8·5 g.), 100—110° (9·3 g.), 110—130° (2·7 g.), and a tarry residue. The three fractions were combined and treated with semicarbazide hydrochloride (15 g.) and sodium acetate (10·7 g.) in boiling alcohol (150 c.c.) and water (150 c.c.) for 15 minutes; water (700 c.c.) was added, and the suspension extracted with ligroin (b. p. 60—80°). The 1-tetralone semicarbazone (total yield, 4·8 g., corresponding to 3·5 g. of 1-tetralone) suspended in the ligroin was filtered off, and the ligroin distilled off, yielding an oil, which was separated into fractions *X*, b. p. up to 100°/5 mm., and *Y*, b. p. 104—108°/5 mm. Fraction *X* (2·8 g.) was heated with sulphur (1·2 g.) at 220—230° for 3 hours, and steam-distillation of the resulting oil gave mainly naphthalene (1·5 g.). Fraction *Y* (8·9 g.) was heated with sulphur (3·5 g.) for 3·5 hours, the temperature being raised slowly to 225—235°; the resulting dark liquid was distilled with steam from 100 c.c. of 20% aqueous sodium carbonate. Naphthalene distilled first, followed by an oil (3·7 g.), b. p. 268—276°/754 mm., separated into fractions, b. p. 270—274° and 274—276°. The former was shown to be mainly 2-*tert.*-butylnaphthalene by oxidation with chromic and acetic acid to 2-*tert.*-butyl-1 : 4-naphthaquinone, m. p. and mixed m. p. 76—77°, whilst the latter fraction was converted in absolute alcohol into a picrate, m. p. 80—95°; fractionation of this picrate from absolute alcohol gave two picrates, *viz.*, (i) 1-*tert.*-butylnaphthalene picrate, pale yellow needles, m. p. 101—102·5° (Found: C, 58·5; H, 4·6; N, 10·7. $C_{14}H_{18}.C_6H_3O_7N_3$ requires C, 58·1; H, 4·6; N, 10·2%), which did not depress the m. p. of the product obtained from 4-*tert.*-butylnaphthalic anhydride, and (ii) 2-*tert.*-butylnaphthalene picrate, yellow needles, m. p. 100—101·5°, not depressed on admixture with an authentic specimen, but which depressed the m. p. of the 1-isomer to 77—95°.

1-tert.-*Butylacenaphthene* (I).—This was prepared in a manner similar to that given for the 3-isomer, but the reaction temperature was kept at 10—15°. The resulting product was fractionated to give acenaphthene (84 g.), b. p. 270°, a mixture (9 g.), b. p. 270—319°, mono-*tert.*-butylacenaphthenes (106 g.), b. p. 319—321°, and a residue which afforded di-*tert.*-butylacenaphthenes (114 g.), b. p. 205—230°/7 mm. Fractional crystallisation of the monobutyl fraction from absolute alcohol gave pure 1-tert.-*butylacenaphthene* (28 g.), m. p. 65—66° (Found: C, 91·3; H, 8·4. $C_{16}H_{18}$ requires C, 91·4; H, 8·6%), the 3-isomer (0·7 g.), and a mixture (*B*) (61 g.), m. p. 48—52° (Found: C, 91·3; H, 8·7%), not depressed in m. p. on admixture with (*A*) in the analogous experiment described above. Buu-Hoï and Cagniant (*Rev. sci.*, 1942, **80**, 176) record a *tert.*-butylacenaphthene, an oil, b. p. 155—160°/0·8 mm., considered by them to be the 1-isomer.

Both (*A*) and (*B*) were shown by oxidation (see later) to contain approximately 25% of 3- and 75% of 1-*tert.*-butylacenaphthene. 1-tert.-*Butylacenaphthene picrate* crystallised from absolute alcohol in orange-red needles, m. p. 93—95° (Found: C, 60·2; H, 4·9; N, 9·3. $C_{14}H_{18}.C_6H_3O_7N_3$ requires C, 60·1; H, 4·8; N, 9·6%), and a *s-trinitrobenzene* complex, golden-orange needles (from alcohol), m. p. 118—119° (Found: C, 63·0; H, 4·9; N, 10·1. $C_{14}H_{18}.C_6H_3O_6N_3$ requires C, 62·4; H, 5·0; N, 9·9%).

The di-*tert.*-butylacenaphthene fraction above gave the 1 : 6-isomer (57 g.), m. p. and mixed m. p. 135—136·5°.

1-tert.-*Butylacenaphthenequinone.*—Sodium dichromate (15 g.) was added all at once to 1-*tert.*-butylacenaphthene (5 g.) in acetic acid (140 c.c.) at 95°, reaction being vigorous and the mixture boiling. After 7 minutes, when reaction had subsided, the mixture was added to ice-water (200 g.) and the resulting solid extracted repeatedly with boiling 5% aqueous sodium carbonate to remove anhydride. The residue was extracted with aqueous sodium metabisulphite and gave 1-tert.-*butylacenaphthenequinone* (0·8 g.), golden-yellow prisms (from alcohol), m. p. 152—154·5° (Found: C, 80·1; H, 5·9. $C_{16}H_{14}O_2$ requires C, 80·7; H, 5·9%). On admixture with the 3-isomeride, m. p. 138—139°, the m. p. was depressed to 111—117°.

1′-tert.-*Butyl*-2 : 7′-*thionaphthenacenaphthenylindigo.*—Prepared in similar manner to the 3′-analogue, the vat *dye* crystallised from toluene in large greenish-black (reflected light) or deep bluish-red (transmitted light) prisms, m. p. 260—262° (Found: C, 77·8; H, 4·7; S, 8·5. $C_{34}H_{18}O_2S$ requires C, 77·8; H, 4·9; S, 8·65%). It dissolves in concentrated sulphuric acid with a green colour, becoming pink on dilution.

2-tert.-*Butylnaphthalic Anhydride.*—Oxidation of 1-*tert.*-butylacenaphthene (15 g.), as for the 4-isomer, is incomplete after 8 hours, much acenaphthenequinone derivative being unoxidised. The *anhydride*, purified through aqueous sodium carbonate, crystallised from acetic acid in needles, m. p. 163—164° (9·4 g., 52%) (Found: C, 75·5; H, 5·5. $C_{16}H_{14}O_3$ requires C, 75·6; H, 5·5%), which depressed the m. p. of the 4-isomer to 130—135°. It was identical with a synthetic specimen (see later).

2-tert.-*Butylnaphthalimide*, prismatic needles (from alcohol), m. p. 201—202°, was prepared by heating the anhydride with aqueous ammonia (*d* 0·88) and alcohol (1 : 1) at 100° (in a sealed tube; essential) for 6 hours (Found: C, 76·3; H, 6·3; N, 5·2. $C_{16}H_{13}O_2N$ requires C, 75·9; H, 5·9; N, 5·5%). The corresponding N-*methylimide*, prepared in an analogous manner, crystallised from aqueous alcohol in needles, m. p. 132—133° (Found: C, 76·4; H, 6·2; N, 5·1. $C_{17}H_{17}O_2N$ requires C, 76·4; H, 6·4; N, 5·2%). Each of these derivatives depressed the m. p. of the respective 4-*tert.*-butyl analogues.

2-tert.-*Butylnaphthalene.*—2-*tert.*-Butylnaphthalic anhydride (5 g.) was distilled with excess of soda-lime, to give 2-*tert.*-butylnaphthalene (2 g.), b. p. 100°/1·8 mm., which yielded a picrate, yellow needles (from absolute alcohol), m. p. 100—101°, not depressed on admixture with an authentic specimen, but depressed to 78—92° on admixture with 1-*tert.*-butylnaphthalene picrate.

Synthesis of 2-tert.-*Butylnaphthalic Anhydride* (cf. Buu-Hoï and Cagniant, *loc. cit.*; Backmann and Sheehan, *J. Amer. Chem. Soc.*, 1941, **63**, 2599, who prepared the ethyl analogue).—Modified methods were used. Pure 2-*tert.*-butylnaphthalene (30 g.), b. p. 102—103°/2 mm. (Bromby *et al.*, *loc. cit.*), was mixed with hydrochloric acid (28 c.c.), acetic acid (24 c.c.), paraformaldehyde (9 g.), and phosphoric acid (14 c.c.) and stirred vigorously at 80—85° for 6 hours. The resulting upper layer was washed twice with water, then with aqueous sodium carbonate, then water, and dissolved in ether (it is important to dry this over potassium carbonate to remove acid and water; otherwise decomposition occurs on distillation). 2-tert.-*Butyl*-1-*chloromethylnaphthalene* (13·5 g.) distilled at 118—126°/0·5 mm. (Found: Cl, 15·6. $C_{15}H_{17}Cl$ requires Cl, 15·3%).

The chloromethyl derivative (18 g.), acetone (180 c.c.), potassium cyanide (17 g.), and water (56 c.c.) were stirred and boiled under reflux for 24 hours. The acetone was removed and the nitrile extracted with ether, isolated, and boiled with hydrochloric acid (60 c.c.), acetic acid (150 c.c.), and water (15 c.c.) for 24 hours. After addition of the mixture to water, the resulting oil was extracted with ether, and the ethereal extract shaken with 10% aqueous sodium hydroxide; the alkali extract was acidified; the resulting oil was extracted with ether, the solvent removed, and the oil distilled, to give a pale brown glass of 2-*tert.*-butyl-1-naphthylacetic acid (10 g.). This was converted by thionyl chloride (+ a little pyridine) in dry ether into the acid chloride, and cyclisation was effected by aluminium chloride (15 g.) in dry benzene (250 c.c.) at 0—5° for 2 hours. 1-*tert.*-Butylacenaphthenone crystallised from alcohol in colourless, prismatic needles, m. p. 91·5—92° (Buu-Hoï and Cagniant give m. p. 92°).

Oxidation of 1 g. with sodium dichromate (3·5 g.) in boiling acetic acid (35 c.c.) for 5 hours gave 2-*tert.*-butylnaphthalic anhydride (1 g., 88%), m. p. and mixed m. p. with that prepared above, 163—164°. Confirmation of this constitution was afforded by preparing the imide, m. p. 201—202°, and *N*-methylimide, m. p. 132—133°, neither of which was depressed in m. p. on admixture with the products already prepared from 1-*tert.*-butylacenaphthene.

Oxidation of Mixed tert.-*Butylacenaphthenes* (A) *and* (B).—(*A*) (10 g.) was oxidised as usual to the mixed *tert.*-butylnaphthalic anhydrides; the first extraction of crude product by boiling 5% aqueous sodium carbonate gave the more soluble 4-*tert.*-butylnaphthalic anhydride (2·2 g.), m. p. and mixed m. p. 165—166°, and three subsequent similar extractions afforded mainly the 2-butylanhydride (2·6 g.), (allowance was made for solubility in dilute hydrochloric acid: 0·18 g. in 1200 c.c.), m. p. and mixed m. p. 163—164°; the insoluble residue was shown to be 1-*tert.*-butylacenaphthenequinone (4·2 g.), but, as expected, no 3-isomeride was isolated. By this means, it is shown that (*A*) and (*B*) (which gave similar results) contain approx. 25% of 3- and 75% of 1-*tert.*-butylacenaphthene.

1 : 6-*Di*-tert.-*butylacenaphthenequinone*.—When oxidised in similar manner to that used for preparing other quinones, 1 : 6-di-*tert.*-butylacenaphthene (15 g.) gave the corresponding *acenaphthenequinone* (4·1 g.), which was purified by chromatography (alumina–benzene), and crystallised from alcohol in yellow needles, m. p. 147—148·5° (Found: C, 81·9; H, 7·4. $C_{20}H_{22}O_2$ requires C, 81·6; H, 7·5%). It would not form a thioindigoid dye when boiled with 3-hydroxythionaphthen in acetic and hydrochloric acids.

When oxidation was prolonged (24 hours), and excess of sodium dichromate (75 g.) was used, 1 : 6-di-*tert.*-butylacenaphthene (15 g.) gave a mixture (15 g.) of the above quinone and 2 : 7-di-*tert.*-butylnaphthalic anhydride; extraction with aqueous sodium carbonate or metabisulphite, crystallisation, or chromatography, did not effect a separation; the mixture, pale yellow crystals, m. p. 127—131°, was used in the following experiment.

2 : 7-*Di*-tert.-*butylnaphthalene*.—The mixture of anhydride and quinone was distilled with soda-lime to yield a solid, which was distilled with steam. The solid part of the distillate crystallised from aqueous alcohol in colourless needles, m. p. 103°, identical with 2 : 7-di-*tert.*-butylnaphthalene prepared from naphthalene or from 3 : 6-di-*tert.*-butylnaphthalic anhydride. Confirmation of this orientation was obtained by conversion into the picrate, yellow needles, m. p. and mixed m. p. 145—146°, and into the complex picrate, orange needles, m. p. 157—158° (cf. Nürsten and Peters, *loc. cit.*).

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363. *The Chemistry of Boron. Part I. The Reactions and Structure of Dihydroxydifluoroboric Acid.*

By L. H. Long and D. Dollimore.

The behaviour of dihydroxydifluoroboric acid, $H_3BO_3F_2$, towards halogenating agents—phosphorus trichloride, phosphorus pentachloride, phosphorus pentabromide, phosphorus tri-iodide, and thionyl chloride—and towards phosphoric oxide has been studied. No reaction was observed with phosphorus trichloride. Otherwise reactions occurred which were characterised by the formation of boron trifluoride or boron phosphate or both.

No single reaction formula can be drawn up to explain the chemical behaviour of dihydroxydifluoroboric acid, and all known facts concerning this compound are best explained on the assumption that the anhydrous acid consists of an equilibrium mixture of associated molecular species in which hydrogen bonding plays an important part. The vapour probably consists of H_2O and $BF_2{\cdot}OH$ molecules, and it is considered improbable that the free $H_3BO_3F_2$ molecule is capable of independent existence.

Although dihydroxydifluoroboric acid, $H_3BO_3F_2$, has been known for a number of years, and some of its properties, particularly its catalytic behaviour, have been studied (Sowa, Kroeger, and Nieuwland, *J. Amer. Chem. Soc.*, 1935, **57**, 454; Kroeger, Sowa, and Nieuwland, *ibid.*, 1937, **59**, 965; Doris, Sowa, and Nieuwland, *ibid.*, 1938, **60**, 656; McGrath, Stack, and McCusker, *ibid.*, 1944, **66**, 1263), much that is fundamental regarding its general chemical nature remains unknown. Accordingly its behaviour with halogenating agents has been examined, namely, with phosphorus trichloride, phosphorus pentachloride, phosphorus pentabromide, phosphorus tri-iodide and thionyl chloride, as well as the behaviour with phosphoric oxide. The results throw some light on the structure of the anhydrous acid. The preparation of dihydroxydifluoroboric acid was accomplished by two of the six methods previously reported (Sowa *et al.*, *loc. cit.*; McGrath *et al.*, *loc. cit.*).

Surprisingly, phosphorus trichloride was found not to react, even at its boiling point, but all the other substances mentioned reacted to different extents, yielding a variety of products. All the volatile products from these reactions were examined and identified by means of high-vacuum technique.

Phosphorus pentachloride reacts with dihydroxydifluoroboric acid in equimolecular ratio with a copious evolution of hydrogen chloride, much of which is evolved in the cold and the remainder only on heating. Boron trifluoride is also liberated, the molecular ratio HCl : BF_3 being approximately 4 : 1. For every three molecules of dihydroxydifluoroboric acid destroyed two of phosphorus oxychloride were formed and one molecule of boron phosphate, which remained behind as an involatile and insoluble residue. The over-all equation

$$3H_3BF_2O_2 + 3PCl_5 \longrightarrow BPO_4 + 2POCl_3 + 2BF_3 + 9HCl$$

accords with the observed facts satisfactorily.

Dihydroxydifluoroboric acid reacts similarly with phosphorus pentabromide, except that no gas is evolved in the cold. On heating, hydrogen bromide and boron trifluoride are evolved, and, in addition to phosphorus oxybromide, boron phosphate is formed as before. An equation similar to that above is therefore postulated.

The reaction between dihydroxydifluoroboric acid and phosphorus tri-iodide is rather different. None occurs in the cold, but on moderately strong heating a reaction sets in which requires two molecules of phosphorus tri-iodide for every three of dihydroxydifluoroboric acid consumed. Hydrogen iodide, boron fluoride, and apparently hydrogen fluoride are liberated, although the latter was not identified as such and was inferred to be among the original products from the heavy vapour-phase attack on the walls of the glass apparatus and from the presence of silicon tetrafluoride. The main reaction is probably

$$3H_3BO_3F_2 + 2PI_3 \longrightarrow [B_2O_3,P_2O_5] + 6HI + BF_3 + 3HF$$

but there are side-reactions, as a small amount of iodine is liberated and a trace of a non-identifiable boron-containing liquid (b. p. ~76°) not attacked by water was obtained. The

postulated residue, $B_2O_3.P_2O_3$ ("boron phosphite," by analogy with boron phosphate, $B_2O_3.P_2O_5$), could not be identified as such since, in common with many tervalent phosphorus compounds, it partly decomposes on strong heating with the liberation of finely divided elementary phosphorus, possibly according to the scheme $5B_2O_3.P_2O_3 \longrightarrow 6BPO_4 + 2B_2O_3 + P_4$. The pale orange residue, which was halogen-free, smelled of phosphorus, ignited on gentle heating in the air, and liberated phosphine with aqueous sodium hydroxide.

Thionyl chloride reacts with dihydroxydifluoroboric acid, but the reaction is rather slow, even at the boiling point of thionyl chloride (76°). Under the conditions adopted, complete reaction was not realised. Four molecules of thionyl chloride react for every three of dihydroxydifluoroboric acid consumed. Hydrogen chloride, sulphur dioxide, and boron fluoride are evolved, while the only solid product is metaboric acid :

$$3H_2BO_2F_2 + 4SOCl_2 \longrightarrow 8HCl + 4SO_2 + 2BF_3 + HBO_2$$

The formation of metaboric acid and not boric oxide has a parallel in the reaction with orthoboric acid, only two-thirds of the water of constitution of which reacts with thionyl chloride at the boiling point of the latter :

$$H_3BO_3 + SOCl_2 \longrightarrow HBO_2 + SO_2 + 2HCl$$

Dihydroxydifluoroboric acid liberates much heat with phosphoric oxide in the cold. No boron trifluoride is liberated, even on heating, but hydrogen fluoride is liberated and is immediately converted into silicon tetrafluoride if glass apparatus is employed. Boron phosphate is also formed, according to the scheme :

$$2H_2BO_2F_2 + P_2O_5 \longrightarrow 2BPO_4 + [H_2O] + 4HF$$

The manner of dehydration is thus different from that occurring with sulphuric acid (Sowa *et al.*, *loc. cit.*), *viz.* :

$$6H_2BO_2F_2 \longrightarrow B_2O_3 + [9H_2O] + 4BF_3$$

The reason for this is doubtless connected with the formation of the very stable lattice compound, boron phosphate, BPO_4.

From the foregoing, it is to be noted that the characteristic feature of the reactions of dihydroxydifluoroboric acid with halogenating agents is the ready production of boron trifluoride. With phosphorus compounds the formation of the lattice compound boron phosphate (cf. Schulze, *Z. physikal. Chem.*, 1934, *B*, **24**, 215) was observed, but otherwise most of the boron was obtained finally as the trifluoride. No other simple or mixed halide of boron was formed in any of the reactions, although such were diligently searched for by chemical tests and by vapour-density and vapour-pressure measurements of the fractions obtained from fractional condensation in vacuum-apparatus.

Thus, dihydroxydifluoroboric acid reacts in a number of different ways : $6H_2BO_2F_2$ may alternatively be given the following " reaction formulæ " :

(1*a*) $B_2O_3.4BF_3.9H_2O$ (1*b*) $2HBO_2.4BF_3.8H_2O$ (1*c*) $2H_3BO_3.4BF_3.6H_2O$

(2) $2B_2O_3.2BF_3.6HF.6H_2O$ (3) $3B_2O_3.12HF.3H_2O$

Formula (1*a*) represents its mode of reaction with phosphorus pentachloride, phosphorus pentabromide, and concentrated sulphuric acid. The variants (1*b*) and (1*c*), which contain the same amount of boron trifluoride, respectively represent the behaviour with thionyl chloride and certain oxygen-containing organic compounds of low molecular weight, namely, alcohols, esters, ketones, aldehydes, and non-cyclic ethers (Kroeger *et al.*, *loc. cit.*). Formula (2) represents the mode of reaction with phosphorus tri-iodide, and formula (3) that with phosphoric oxide. It follows that no single reaction formula accounts for the general chemical behaviour, indicating that more than one molecular species may be present in the anhydrous acid : many of the reactions, particularly the comparatively ready liberation of boron trifluoride, are more easily explained on the assumption that the acid is to a slight extent in equilibrium with boron trifluoride hydrate on the one hand, and boric acid on the other, *e.g.* :

$$3H_2BO_2F_2 \rightleftharpoons 2BF_3.2H_2O + HBO_2$$

or

$$3H_2BO_2F_2 \rightleftharpoons BF_3.2H_2O + BF_3.H_2O + H_3BO_3$$

It is relevant that $BF_3,2H_2O$ is a strong acid and is to be written $[H_3O][BF_3{\cdot}OH]$ (Meerwein and Pannwitz, *J. pr. Chem.*, 1934, [ii], **141**, 123; Klinkenberg and Ketelaar, *Rec. Trav. chim.*, 1935, **54**, 959), but from its behaviour it must be regarded as being partly dissociated into an equilibrium mixture of hydroxyfluoroboric acids (McGrath *et al.*, *loc. cit.*). Moreover, Wamser (*J. Amer. Chem. Soc.*, 1948, **70**, 1209) has observed that the acid $H[BF_3{\cdot}OH]$ is a particularly stable intermediate equilibrium stage in the reaction between boric acid and hydrogen fluoride.

Dihydroxydifluoroboric acid is stated to behave as a strong monobasic acid and the formula of the dissociated acid has been given as $H[HO{-}\overset{\overset{F}{|}}{B}{-}OH]$ (or perhaps more correctly, in aqueous solution $[H_3O][HO{-}\overset{\overset{F}{|}}{B}{-}OH]$) as suggested by Sowa *et al.* This representation is however not permissible for the anhydrous acid, since this has a conductivity only of the order of that of concentrated sulphuric acid, in which free protons do not occur in the liquid as such but are absorbed into the structure of the acid, as shown by *X*-ray studies (Finbak, *Tids. Kjemi Bergvesen Met.*, 1943, **3**, 40). The suggestion by Kroeger *et al.* that the proton of the dihydroxydifluoroboric acid is co-ordinated to the oxygen (or alternatively to the fluorine), so that molecules such as $H{-}\overset{+}{O}{-}\overset{\overset{F}{|}}{\overset{-}{B}}{-}O{-}H$ are present does not do more than partial justice to the facts. First, it is very doubtful if single molecules of $H_3BO_2F_2$ are any more capable of independent existence than those of, say, HBF_4. Secondly, apart from the fact that many compounds containing both hydrogen and fluorine are associated, the presence of the hydroxyl groups would lead one to expect marked association. It is moreover hard to see how hydrogen bonds involving both the oxygen and the fluorine of the various molecular species present could fail to be formed, although the literature does not even mention the possibility of hydrogen bonding in this connexion. That hydrogen bonds do indeed occur is strongly indicated by the physical properties of the anhydrous acid, namely, high viscosity, high density, high boiling point relative to the size of the molecule, and high latent heat of vaporisation. For a compound containing only boron, oxygen, fluorine, and hydrogen, the surprisingly high density of 1·66, which approaches that of orthophosphoric acid, is especially noteworthy, the more so since the *a priori* possibilities of hydrogen-bond formation are about the same as in phosphoric and sulphuric acids, which dihydroxydifluoroboric acid resembles in viscosity (as well as in electrical conductivity). In both sulphuric and phosphoric acid, as in water, hydrogen bonding is known to lead to an O—H—O distance of 2·85 A. (Finbak, *loc. cit.*; Bastiansen and Finbak, *Tids. Kjemi Bergvesen Met.*, 1944, **4**, 40), and in the case of dihydroxydifluoroboric acid we now have the evidence of the increased stability of the hydroxyl groups and hence reduced reactivity which would arise from quite firm hydrogen bonding. Taken as a whole, the reactions here reported with halogenating agents are remarkably sluggish, while phosphorus trichloride does not react at all under the conditions tried. The hydroxyl groups are thus even less reactive than those in orthoboric acid, which reacts, for instance, with phosphorus trichloride on heating and more readily with thionyl chloride. The results of *X*-ray studies and Raman spectroscopy are awaited with interest.

Finally, the presence of small amounts of the products of *non-electrolytic* dissociation must be admitted, since the vapour density is almost exactly half that required by the formula $H_3BO_2F_2$ (Sowa *et al.*). It follows that the total pressure of the products of dissociation reaches one atmosphere at 160°, which is therefore not a true boiling point but a dissociation equilibrium temperature. Sowa *et al.* suggest that the molecular species present in the vapour phase are $HF + BF(OH)_2$, but were this the case it is hard to see why the hydrogen fluoride does not attack the glass walls of the distilling apparatus. In fact, dihydroxydifluoroboric acid can be distilled in ordinary glass apparatus without etching, and no decomposition is observed beyond the deposition of a very small amount of an unidentified white solid on the walls of the condenser (cf. Sowa *et al.*, *loc. cit.*). A more probable alternative, therefore, is the equilibrium

$$\underset{\text{(liquid)}}{H_3BO_2F_2} \rightleftharpoons \underset{\text{(vapour)}}{H_2O + BF_3{\cdot}OH}$$

the members on the right-hand side also being able to participate in hydrogen bonding in the liquid phase. Here again there is a parallel with sulphuric acid, for according to the Brønsted–Lowry concept of an acid, the water molecules will pick up protons from further molecules of

the acid and give rise to hydroxonium ions. Since, as in the case of sulphuric acid (Finbak, *Avh. Norske Videnskaps-Akad. Oslo*, I. *Mat.-naturv. Klasse*, 1944, No. 6), the number of protons transferred is limited by the number of water molecules present, and since the conductivity of anhydrous dihydroxydifluoroboric acid is appreciable, it is to be presumed that the foregoing dissociation is not negligible in the liquid phase, even at room temperature.

Experimental.

Preparation of Dihydroxydifluoroboric Acid.—The method mainly adopted was the action of boron trifluoride on orthoboric acid at room temperature, $2BF_3 + 4H_3BO_3 \longrightarrow 3HBO_3 + 3H_3BO_3F_3$. Gaseous boron trifluoride was passed over solid boric acid until the latter became syrupy. On subsequent distillation, dihydroxydifluoroboric acid came over at 160°. The yield was almost 100% based on the boric acid.

An alternative method consisting of separating dihydroxydifluoroboric acid from a reaction mixture of calcium fluoride, boric oxide, and a limited quantity of concentrated sulphuric acid did not prove to be so satisfactory, and in view of the rather poor yield was abandoned.

Redistilled dihydroxydifluoroboric acid had d^{20} 1·6605 (cf. d^{25} 1·6569, d^{30} 1·6539 reported by Sowa *et al.*, *loc. cit.*; cf. Kroeger *et al.*, *loc. cit.*).

Reactions of Dihydroxydifluoroboric Acid with Halogenating Agents.—General. In each case, attempts were first made to carry out the reaction at room temperature, heat being applied subsequently. All volatile products were collected, the liquids being condensed by means of a Liebig condenser and substances boiling below room temperature in a liquid-oxygen trap for subsequent examination by high-vacuum technique. The solid residue left in the reaction flask was recovered and investigated, although it was not always possible to identify it completely.

With phosphorus trichloride. Dihydroxydifluoroboric acid (41·6 g.) and phosphorus trichloride (45·8 g.) were mixed. The mixture separated into two layers. No visible reaction occurred in the cold or on heating. The reactants were finally distilled off unchanged, and not more than a trace of hydrogen chloride was collected in the liquid-oxygen trap.

With phosphorus pentachloride. Preliminary experiments, in which excess of phosphorus pentachloride was employed, indicated reactions in equimolecular proportions. The dihydroxydifluoroboric acid was run on to phosphorus pentachloride. A copious evolution of hydrogen chloride occurred in the cold. When the mixture was heated, further hydrogen chloride was evolved and some phosphorus oxychloride distilled. The contents of the liquid-oxygen trap gave positive tests for boron, fluorine, and chlorine.

In the next experiment, dihydroxydifluoroboric acid (24 g.) in slight excess was added to phosphorus pentachloride (47 g.). The excess of acid was subsequently recovered unchanged. The condensate in the liquid-oxygen trap was transferred to a vacuum apparatus. Its vapour pressure lay between that of hydrogen chloride (b. p. −85°) and that of boron trifluoride (b. p. −101°). Successive head fractions were pumped off and the vapour density of each measured by Martin and Dial's procedure (*J. Amer. Chem. Soc.*, 1950, **72**, 852). The vapour density of the successive fractions dropped from 24·89 to 19·90 (BF_3, 33·9; HCl, 18·25). These experiments indicated a BF_3 : HCl molar ratio of approx. 1 : 4 and demonstrated the absence of heavier and less volatile compounds such as boron trichloride or boron fluorochloride. 24·2 g. of impure phosphorus oxychloride were recovered. The residue was a light-grey powder containing boron and phosphorus but no halogen, insoluble in acids and dilute alkali, but partly soluble in hot concentrated sodium hydroxide solution; in this it behaved like boron phosphate.

With phosphorus pentabromide. Preliminary experiments indicated that the reaction proceeded as with phosphorus pentachloride, except that no appreciable quantity of hydrogen bromide was evolved until heating was commenced. Dihydroxydifluoroboric acid (13 g.) and phosphorus pentabromide (65 g., equimolecular quantity) were warmed until the evolution of gas was complete. Subsequent attempts to distil off the phosphorus oxybromide formed were only partly successful, some remaining with the solid residue. The latter, when washed free from the oxybromide, proved to have the same inert properties as in the case of the experiment with phosphorus pentachloride and was to all appearances boron phosphate. The condensate in the liquid-oxygen trap was mainly hydrogen bromide with a smaller quantity of boron trifluoride. Complete separation was not effected, but, on subsequent fractional condensation in vacuum apparatus, the boron and fluorine collected in the lighter (vapour density, 39·56) and more volatile head fraction, while the tail fraction gave negative tests for both fluorine and boron and behaved as pure hydrogen bromide (vapour density, 40·64). There were no indications of the formation of boron bromide or mixed halides of boron.

With phosphorus tri-iodide. Preliminary experiments indicated that no reaction occurred in the cold but that, on heating, hydrogen iodide was evolved, the molecular ratio of $H_3BO_3F_3$: PI_3 being 3 : 2. Accordingly, dihydroxydifluoroboric acid (15 g.) was heated with phosphorus tri-iodide (48 g.). The gas evolved proved, on examination in vacuum apparatus, to be a mixture of hydrogen iodide, boron trifluoride, and silicon tetrafluoride. There was an appreciable quantity of the latter, which appeared to have arisen through the secondary attack of hydrogen fluoride on the glass apparatus, which was severely etched. Two very small liquid fractions were obtained. The first (b. p. 76°) (about 0·2 c.c.) was violet through dissolved iodine. The amount was too small to identify. It was denser than water, with which it was immiscible and did not appear to react. It dissolved in sodium hydroxide solution, however, and the resulting solution gave a positive test for boron (as well as for iodine). The second liquid fraction (about 0·5 c.c.) was unchanged dihydroxydifluoroboric acid (b. p. 160°). The solid residue was yellow-brown and contained phosphorus and boron, but no halogen. It smelled of phosphorus, ignited on heating and liberated phosphine on treatment with sodium hydroxide. It could not be identified, but part of it was insoluble and behaved like boron phosphate. It appeared that the elementary phosphorus in the residue was liberated only on strong heating by virtue of a secondary

reaction, since the residue from the preliminary experiment, which had not been so strongly heated, was light orange and liberated a much smaller proportion of phosphine on treatment with alkali.

With thionyl chloride. Thionyl chloride was purified by distillation over quinoline and linseed oil. In one experiment, the chloride (57·1 g.) and dihydroxydifluoroboric acid (30·0 g.) were mixed. The two liquids separated into two layers and appeared not to react in the cold, but after 12 hours a considerable quantity of condensate had collected in the liquid-oxygen trap. On heating, the reaction proceeded more rapidly, but was still incomplete after 1 hour, during which the unchanged portions were distilled over. The condensate in the liquid-oxygen trap was shown by fractional condensation in vacuum-apparatus to consist of a mixture of boron trifluoride, hydrogen chloride, and sulphur dioxide. The quantities of reactants recovered unchanged were 10·1 g. of thionyl chloride and 6·8 g. of dihydroxydifluoroboric acid; *i.e.*, 47·0 g. of thionyl chloride had reacted with 23·2 g. of dihydroxydifluoroboric acid, which corresponds approximately to the molecular ratio $4SOCl_2 : 3H_2BO_2F_2$. The residue was a white powder (3·8 g.), containing boron, but no sulphur or halogen. It was completely soluble in water giving an acidic solution, a weighed quantity titrating with sodium hydroxide and glycerol as metaboric acid (35·00 g./l. by weight, 35·22 g./l. by titration).

In another experiment it was demonstrated that thionyl chloride at its b. p. (76°) converts orthoboric acid not into metaboric acid, but into boric oxide. Orthoboric acid (20·0 g.) was refluxed with excess of purified thionyl chloride for a considerable period after the evolution of hydrogen chloride and sulphur dioxide had ceased (24 hours in all). After removal of the excess of thionyl chloride and evacuation, metaboric acid (14·2 g.) was obtained (theory, 14·18 g.).

With phosphoric oxide. The quantities of dihydroxydifluoroboric acid and phosphoric oxide used were 84 g. and 71 g. respectively (B : P ratio = 1 : 1). The liquid dihydroxydifluoroboric acid was added slowly to the oxide. A violent exothermic reaction took place, but no gas was evolved at this stage. On subsequent heating, a white solid collected in the liquid-oxygen trap. The condensate contained fluorine, but no boron or phosphorus, and by its sublimation point, vapour density, and chemical behaviour was proved to be practically pure silicon tetrafluoride, this probably having arisen through the primary liberation of hydrogen fluoride (severe etching). The residue contained boron and phosphorus, but no fluorine. The insoluble portion, after being washed, had the properties of boron phosphate.

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UNIVERSITY COLLEGE, EXETER. [*Received, March 6th*, 1951.]

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364. *A Theoretical Treatment of the Diels–Alder Reaction. Part III.* Equilibria for Aromatic Hydrocarbons.*

By R. D. BROWN.

The localization theory of the Diels–Alder reaction, developed in Parts I and II (*J.*, 1950, 691, 2730), is applied to the equilibrium set up between some anthracene derivatives and maleic anhydride. It is shown that equilibria relative to a reference hydrocarbon can be predicted quantitatively for rigid, conjugated systems, energies being computed by the usual L.C.A.O. approximation including overlap. Neglect of overlap materially affects the agreement. The effect of some neglected factors upon the accuracy of the present theory is discussed.

IN Parts I and II (*J.*, 1950, 691, 2730) the localization theory of organic reactions was used to discuss the Diels–Alder properties of polycyclic hydrocarbons and arylpolyenes. Particularly in the case of the former it was shown that the para-localization energies were in excellent accord with the observed reactivities, but attention was directed mainly to experimental data which probably indicated rates of reaction. It will now be shown that quantitative agreement with experiment is obtained for the Diels–Alder equilibria which are set up by many polycyclic aromatic hydrocarbons (Bachmann and Kloetzel, *J. Amer. Chem. Soc.*, 1938, **60**, 481).

The simplifying assumptions made when considering relative rates of reaction (Parts I and II) are equivalent to supposing that the entropy of activation remains constant. Similarly, for the present considerations of equilibria we may suppose, in the absence of more detailed information, that the entropy of reaction is substantially independent of the hydrocarbon involved, differences in the free energy of reaction for different hydrocarbons being predominantly due to differences in the heats of reaction. This is the more likely if the hydrocarbons have similar structures, which indeed is true of the compounds considered below.

* Part II, *J.*, 1950, 2730.

In good approximation, the differences in the heats of reaction will be represented by differences in para-localization energies, so we may write

$$\Delta G - \Delta G_0 = P - P_0 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

which of course is equivalent to a description of the equilibria in terms of the changes in resonance energies. The validity of this equation, when P and P_0 are computed by the L.C.A.O. approximation, may be tested by use of Bachmann and Kloetzel's data (*loc. cit.*) for the % adduct in equilibrium with the hydrocarbon and maleic anhydride. Their experimental results are reproduced in Table I. The concentration, which enters into the equilibrium constant owing to the different numbers of reactant and product molecules, has been computed by assuming that all solutions were equimolar in the reactants and contained 0·1 g. of hydrocarbon in 2 ml. of solvent, as mentioned by Bachmann and Kloetzel. Unfortunately these authors give no indication of the precision with which the solutions were prepared.

TABLE I.

Hydrocarbon.	Molar concn., c.	Molar fraction of adduct at equilibrium, x.	$d(\ln K)/dx$.*
Anthracene	0·28	0·99	95
1 : 2-Benzanthracene	0·22	0·84	13
1 : 2-5 : 6-Dibenzanthracene	0·18	0·30	6·2

T = ca. 140°; RT = 0·82 kcal. * $K = \dfrac{x}{c(1-x)^2}$.

Dibenzanthracene was chosen as standard since for it $d(\ln K)/dx$ has the smallest value so that a given error in x_0 will produce the smallest relative error in K. Values of x for the other hydrocarbons were computed by use of equation (1) and the thermodynamic relation $RT \ln (K/K_0) = \Delta G_0 - \Delta G$. The values of P and P' (for symbolism see Part I) were converted into kcals. by use of the values previously used (Part II), *i.e.*, $\beta = -17.1$ kcal., $\gamma = -33.6$ kcal.

The relevant values of the para-localization energies and the equilibrium molar fractions of adduct, $x(p)$, $x(p')$, calculated by using dibenzanthracene as standard are listed in Table II.

TABLE II.

Hydrocarbon.	p.	p'.	$x(p)$.	$x(p')$.	$x_{exp.}$.
Anthracene	3·3137	2·0744	0·87$_3$	0·97$_0$	0·99
Benzanthracene	3·4180	2·1729	0·65$_8$	0·83$_5$	0·84
1 : 2-5 : 6-Dibenzanthracene	3·5140	2·2630	(0·30)	(0·30)	0·30
1 : 2-3 : 4-Dibenzanthracene	—	2·2442	—	0·42	—
1 : 2-7 : 8-Dibenzanthracene	—	2·2618	—	0·31	—
Naphthalene	—	2·3964	—	0·005$_6$	—

$p = -P/\beta$. $p' = -P'/\gamma$.

It is evident that $x(p)$ is only qualitatively in agreement with experiment. On the other hand $x(p')$ is in good *quantitative* accord with $x_{exp.}$, the experimental uncertainty in the latter, according to Bachmann and Kloetzel, being 0·01—0·02.

Further corroborative evidence for the surprising precision of the L.C.A.O. approximation for the ground states of conjugated hydrocarbons, the overlap integral being retained for nearest neighbours, is found in a study of the relative rates of addition of osmium tetroxide to aromatic hydrocarbons (Brown, *J.*, 1950, 3249).

It would of course be desirable to extend the comparison with experiment to further polycyclic hydrocarbons. With this in view values of $x(p')$ for naphthalene and two additional dibenzanthracenes are given in Table II, the results applying to the experimental conditions employed by Bachmann and Kloetzel. As mentioned below, naphthalene may not prove as satisfactory as the other hydrocarbons because the adduct will contain an isolated double bond in place of an aromatic system in the other adducts.

The Effects of Errors in x_0 *and* $p_0' - p'$.—The calculated values of $x(p')$ in Table II will of course be affected by errors in the theoretical calculation of $p_0' - p'$, and by any error involved in taking x_0 as 0·30. Values of dx/dx_0 and $dx/d(p_0' - p')$ are given in Table III for the compounds listed in Table II.

TABLE III.

Hydrocarbon.	dx/dx_0.	$dx/d(p_0' - p')$.	Hydrocarbon.	dx/dx_0.	$dx/d(p_0' - p')$.
Anthracene	0·06$_8$	0·43	1 : 2-3 : 4-Dibenzanthracene	1·1	7·0
Benzanthracene	0·4$_7$	3·1	1 : 2-7 : 8-Dibenzanthracene	1·0	6·7
Naphthalene	0·03	0·23			

It is seen from Table III that in order to obtain agreement between $x(p')$ and $x_{exp.}$ to 0·01, the quantity $p_0' - p'$ must be correct to 0·02 for anthracene and 0·003 for benzanthracene. When it is recalled that p_0' and p' are calculated as differences in π-electron energies, which for dibenzanthracene are of the order of 20 (in units of γ), the self-consistency of the L.C.A.O. calculations required to obtain the agreement found in Table II seems quite extraordinary.

Factors Neglected in the Present Treatment.—The localization treatment of the Diels–Alder reaction does not distinguish between *endo*- and *exo*-forms of the adduct with respect to equilibrium concentrations (or rates of formation). However, it is often the case that one stereoisomer is formed exclusively, indicating that factors not so far taken into account in the localization theory can be decisive in determining the relative rates of formation of the two possible products. It seems certain that the difference in stability of the two stereoisomers is due to induction forces of the type responsible for molecular binding between aromatic compounds and polynitro-compounds (Briegleb, "Zwischenmolekulare Kräfte und Molekülstrüktur," Enke, 1937).

When the diene is a polycyclic hydrocarbon the relative stabilities of the two stereoisomers will be determined by the difference in interaction energy of the maleic anhydride multipole and the two smaller cyclic systems on either side of the ring undergoing addition. Since induction forces fall off very rapidly with distance the interactions will be very similar even when the cyclic systems are rather different (*e.g.* benzene and anthracene). The present results and the qualitative success of the theory for polycyclic systems (Part I) support this conclusion.

However, in the case of 1 : 4-addition to naphthalene, for example, in the *endo*-form the interaction is between the maleic anhydride residue and benzene, whilst in the *exo*-form it is between the maleic anhydride residue and ethylene. Here some difference in energy might be expected. For this reason naphthalene may not prove as useful a test of the quantitative agreement between theory and experiment as larger polycyclic hydrocarbons. The variation in induction forces may also be important in arylpolyenes, such as those considered in Part II, and for this reason the localization theory may not prove so successful for these compounds even when the difficulties associated with partial rotation about bonds of low mobile order are resolved.

Another factor neglected in the present treatment is the variation of the resonance integral with bond order. In the case of polycyclic hydrocarbons this variation is not so important because the variation in mobile order is not very great, but in the case of polyenes and arylpolyenes the variation is greater. The allowance for this variation in the calculation of π-electron energies is very tedious and it seems important to establish first how reliable are the present simplified molecular-orbital calculations by further quantitative investigations of equilibria before introducing further refinements into the theoretical treatment.

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NOTES.

365. *Characteristic Absorption Bands in the* 10-μ. *Region of the Infra-red Spectra of* cyclo*Paraffin Derivatives.*

By L. W. Marrison.

Absorption bands in the infra-red region which appear to be characteristic of *cyclo*paraffinic structures have been reported by Derfer, Pickett, and Boord (*J. Amer. Chem. Soc.*, 1949, **71**, 3482) for *cyclo*propane homologues and monoalkyl*cyclo*butanes. An examination of published data of the absorption compounds in the 9—11-μ. region, supplemented by measurements made in this Laboratory, provides evidence for rather more extensive generalisation.

The observation by Derfer *et al.* (*loc. cit.*) that the homologues of *cyclo*propane have a band at 1000—1020 cm.$^{-1}$ applies also to vinyl*cyclo*propane (Van Wolkenberg *et al.*, *ibid.*, p. 3595), but not to *cyclo*propane itself, which has a band at 1028 cm.$^{-1}$.

The band between 909 and 917 cm.$^{-1}$, which occurs in the spectra of all monoalkyl*cyclo*butanes (Derfer *et al.*, *loc. cit.*) is not present in either methylene- or octafluoro-*cyclo*butane. A band between 960 and 1000 cm.$^{-1}$ is, however, present in the published spectra of all *cyclo*butane compounds ("Catalog of Infra-Red Spectrograms," A.P.I. Research Project 44, National Bur. Standards).

The spectra of all *cyclo*pentane derivatives have a band whose average position is at 977 cm.$^{-1}$. The variation in published data is so wide, however, that the significance of its presence or absence in an unknown compound is negligible (*e.g.*, *n*-butyl*cyclo*pentane 937; ethyl*cyclo*pentane 1020 cm.$^{-1}$).

The published spectra of *cyclo*hexane derivatives show two bands, one between 952 and 1005 cm.$^{-1}$, and the other between 1000 and 1055 cm.$^{-1}$. Among the 50 compounds listed there are only two exceptions: *cyclo*hexane itself (1041 cm.$^{-1}$ only), and the β-isomer of 1 : 2 : 3 : 4 : 5 : 6-hexachloro*cyclo*hexane (1055 cm.$^{-1}$ only) (*op. cit.*, Thompson, *J.*, 1948, 1432; Nielsen *et al.*, *Analyt. Chem.*, 1949, **21**, 369; Grédy, *Compt. rend.*, 1934, **198**, 89; Sheppard, *Trans. Faraday Soc.*, 1950, **46**, 423). The following data (cm.$^{-1}$) were obtained in this Laboratory:

*cyclo*Hexanol	961; 1020
Chloro*cyclo*hexane	995; 1018
α-1 : 2 : 3 : 4 : 5 : 6-Hexachloro*cyclo*hexane	952; 1044
β- " " "	1055
γ- " " "	952; 1025
δ- " " "	955; 1036
α-Heptachloro*cyclo*hexane	957; 1005
β- " "	966; 1013
δ- " "	960; 1027

*cyclo*Hexanone and its derivatives, whose spectra have been described by Lecomte (*Compt. rend.*, 1945, **221**, 50) and Cherrier (*ibid.*, 1947, **225**, 1063), show several deviations from the generalisation proposed and it is clear that it cannot be applied to these compounds.

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WIDNES LABORATORY, WIDNES. [*Received, November 18th*, 1950.]

366. *Organocobalt Compounds.*

By D. A. E. BRIGGS and J. B. POLYA.

THE preparation and properties of some organocobalt compounds have been described by Ingles and Polya (*Nature*, 1949, **164**, 447; *J.*, 1949, 2280). Circumstances have prevented a systematic extension of this work but the present note supplements previous information on some naphthylcobalt halides.

When α- and β-naphthylcobalt tri-iodides were prepared by the previously described methods except that highly purified solvents were used in the present experiments, light petroleum caused incomplete precipitation. Precipitation with dioxan afforded reduced but satisfactory yields and the filtrates gradually deposited small amounts of R_2CoI_3. In one case a somewhat impure material of the approximate formula R_3CoI_3 was obtained which recalls the $R_3Co_2Br_3$ previously described. These findings confirm the view that dioxan decomposes organocobalt halides of the type $RCoX_3$ to R_2CoX_3 which occasionally permits the isolation of $RCoX_3.R_2CoX_3$.

Reaction of the naphthylcobalt tri-iodides with methyl iodide gave dinaphthyls in place of the expected methylnaphthalenes. Acetyl chloride gave very poor yields of acetylnaphthalenes, but $(\beta\text{-}C_{10}H_7)_3Co_2I_3$ gave 47% of the ketone. α-Naphthylcobalt tri-iodide and benzoyl chloride gave good yields of 1-benzoylnaphthalene, but the reaction failed with the β-isomer and with $(\beta\text{-}C_{10}H_7)_3Co_2I_3$.

Experimental.—By use of pure solvents and of dioxan for precipitation were obtained, on a 0·1 molar scale:

(*a*) α-Naphthylcobalt tri-iodide, yellowish-green, decomp. 153° (48%) (Found: C, 21·0; H, 1·4; I, 66·4. Calc. for $C_{10}H_7I_3Co$: C, 21·0; H, 1·2; I, 67·5; Co, 10·3%), and di-α-naphthylcobalt di-iodide (2%) (Found: I, 45·1; Co, 9·7. Calc. for $C_{20}H_{14}I_2Co$: I, 44·8; Co, 10·3%).

(*b*) β-Naphthylcobalt tri-iodide, yellowish-green, decomp. 164—166° (15%) (Found: C, 20·8; H, 1·4; I, 67·7; Co, 10·0%), di-β-naphthylcobalt di-iodide (1%) (Found: I, 44·3; Co, 10·7%), and *tri-β-naphthyldicobalt pentaiodide*, greyish-green (15%) (Found: C, 30·2; H, 2·4; I, 53·3; Co, 10·8. $C_{30}H_{21}I_5Co_2$ requires C, 31·6; H, 2·3; I, 55·8; Co, 10·3%).

Reaction with acetyl chloride. When α-naphthylcobalt tri-iodide (1·0 g.) and acetyl chloride (5·0 c.c.) were mixed, cobalt halides and iodine were formed at once. After being kept for 1 hour at room temperature and then heated for 2 hours on the water-bath, the mixture was treated with ice-water (15 c.c.) and extracted with ether. The extract was washed successively with aqueous sodium carbonate and thiosulphate and with water and then evaporated. The residual brown oil gave 1-acetylnaphthalene semicarbazone, m. p. 235° (from ethanol) (3—4%). Similarly was obtained 2-acetylnaphthalene, m. p. 52—53° (semicarbazone, m. p. 236—237°), in 6—8% yield from $RCoI_2$ or 47% yield from R_2CoI_3.

Reaction with benzoyl chloride. 1-Naphthylcobalt tri-iodide (1·0—5·0 g.) and benzoyl chloride (5—20 c.c.) were set aside for 1 hour and then refluxed gently for 90 minutes. The product was extracted with ether and washed as above. The residues from the ethereal solution were recrystallised three times from aqueous alcohol and afforded 1-benzoylnaphthalene, m. p. 72—73°, identified as the oxime, m. p. 140—141°, in yields which varied between 54 and 75% in a number of experiments.

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367. 4 : 6-*Dimethyl* β-*Methylglucoside and Some Derivatives of* β-*Methylglucoside.*

By J. C. DENNISON and D. I. MCGILVRAY.

4 : 6-DIMETHYL β-METHYLGLUCOSIDE was synthesised by Bell and Synge (*J.*, 1937, 1711) by methylation of β-methylglucoside 2 : 3-dinitrate and subsequent hydrolysis. Later, Bell and Lorber (*J.*, 1940, 453) prepared the α-isomeride from 2 : 3-dibenzyl α-methylglucoside; and application of this synthesis in a slightly modified form has now enabled us to obtain 4 : 6-dimethyl β-methylglucoside in a higher-melting form than previously reported.

Experimental.—2 : 3-*Dibenzyl* 4 : 6-*benzylidene* β-*methylglucoside.* 4 : 6-Benzylidene β-methylglucoside (cf. Mathers and Robertson, *J.*, 1933, 698) (30 g.), powdered potassium hydroxide (25 g.), and benzyl chloride (100 ml.) were stirred in a closed vessel at 100° for 5 hours. After isolation and purification (cf. Bell and Lorber, *loc. cit.*), the *dibenzyl* compound crystallised from ethanol (95%) as fine needles, m. p. 119—120°, $[\alpha]_D^{20}$ −35·8° (*c*, 3·02 in chloroform) (Found: OMe, 6·6. $C_{28}H_{30}O_6$ requires OMe, 6·7%).

2 : 3-*Dibenzyl* β-*methylglucoside.* This was prepared from the benzylidene derivative in 95% yield, by the procedure of Bell and Lorber (*loc. cit.*). This *glucoside* crystallised from light petroleum (b. p. 60—80°) in fine needles, m. p. 122—123°, $[\alpha]_D^{20}$ −13·3° (*c*, 2·7 in chloroform) (Found: OMe, 8·8. $C_{21}H_{26}O_6$ requires OMe, 8·2%).

2 : 3-*Dibenzyl* 4 : 6-*dimethyl* β-*methylglucoside.* The foregoing compound (7·0 g.) was twice methylated with Purdie's reagents. The *product* (7·6 g.) crystallised overnight in a vacuum-desiccator and had m. p. 40—41°, $[\alpha]_D^{20}$ +32·0° (*c*, 2·52 in chloroform) (Found: OMe, 23·0. $C_{23}H_{30}O_6$ requires OMe, 23·1%).

4 : 6-*Dimethyl* β-*methylglucoside.* The benzyl groups were removed from the benzyl ether (7·6 g.) with sodium in ethanol (cf. Bell and Lorber, *loc. cit.*). The crude product (2·7 g.; m. p. 69—71°), after recrystallisation from light petroleum (b. p. 60—80°), melted at 77—79° and had $[\alpha]_D^{20}$ −27·0° (*c*, 2·74 in chloroform) (Found: OMe, 40·5. Calc. for $C_9H_{18}O_6$: OMe, 41·8%). Bell and Synge (*loc. cit.*) and Peat and Wiggins (*J.*, 1938, 1813) gave m. p. 50—52°, and Reeves (*J. Amer. Chem. Soc.*, 1949, **71**, 217) stated that the m. p. was initially 52—55°, but that after being kept the compound had m. p. 67—68°. The properties of the 2 : 3-ditoluene-*p*-sulphonyl derivative agreed with those recorded by other workers.

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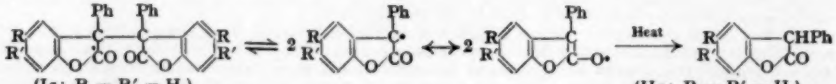
URMSTON, NR. MANCHESTER. [*Received, February 24th*, 1951.]

368. *Reactions of Diaryldicoumaranonyls and* 2 : 2′-*Diphenylthioindigo-white.*

By AHMED MUSTAFA and AHMED MEDHAT ISLAM.

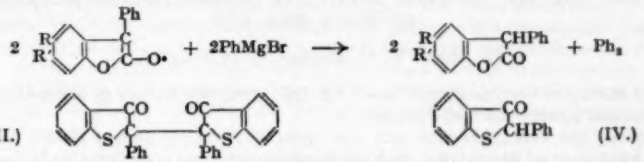
SCHÖNBERG AND MUSTAFA (*J.*, 1949, 889) have found that 2 : 2′-diketo-3 : 3′-diphenyl-3 : 3′-dicoumaranyl (I*a*) and 2 : 2′-diphenylthioindigo-white (III) form the corresponding reduction products, (II*a*) and (IV), when heated at 270° without a solvent. The analogues (I*b*, *c*, and *d*) are known to form, in solution, free radicals that may be regarded as resonance hybrids (see below) (Lõwenbein, *Ber.*, 1925, **58**, 601; Arventi, *Ann. Sci. Univ. Jassy*, 1938, **24**, 219). When heated at 270°, they too gave the reduction products, namely, (II*b*, *c*, and *d*), which we believe to be produced from the free radicals by disproportionation (cf. Schönberg and Mustafa, *loc. cit.*).



(I*a*; R = R′ = H.)
(I*b*; R = H; R′ = Me.)
(I*c*; R = Me; R′ = H.)
(I*d*; R = Cl; R′ = H.)

(II*a*; R = R′ = H.)
(II*b*; R = H, R′ = Me.)
(II*c*; R = Me, R′ = H.)
(II*d*; R = Cl, R′ = H.)

When a benzene solution of (I*a*) was added to an ethereal phenylmagnesium bromide solution and the mixture was decomposed with aqueous ammonium chloride, (II*a*) was obtained in almost quantitative yield, together with diphenyl, whereas (I*a*) was recovered unchanged when shaken with an aqueous ammonium chloride solution for 3 hours at room temperature [cf. the action of phenylmagnesium bromide on *s*-tetraphenyldibenzoylethane (Löwenbein and Schuster, *Annalen*, 1930, **481**, 106)]. The action of phenylmagnesium bromide is similar with (I*b*, *c*, and *d*) and with (III). This is an example of reductive fission of the C–C linkage by the Grignard reagent (cf. Mustafa, *J.*, 1949, 1662).



Experimental.—Thermal decompositions. (*a*) 2 : 2′-Diketo-6 : 6′-dimethyl-3 : 3′-diphenyl-3 : 3′-dicoumaranyl (I*b*) (1 g.) (Löwenbein, *loc. cit.*) was heated in a test-tube connected by a bent tube to a test-tube cooled by ice–salt. Dry carbon dioxide was passed through the apparatus. Pyrolysis (bath-temp. 270°) was carried out for ½ hour. Colourless crystals which appeared on the walls of both test-tubes were collected and recrystallised from ethyl alcohol; they had m. p. 122° (0·8 g., *ca.* 80%) and were shown to be the lactone of 6-methyl-3-phenylcoumaran-2-one (II*b*) (identity : mixed m. p. and colour reaction with sulphuric acid; Bistrzycki and Flatau, *Ber.*, 1897, **30**, 130).

(*b*) When 2 : 2′-diketo-5 : 5′-dimethyl-3 : 3′-diphenyl-3 : 3′-dicoumaranyl (I*c*) (1 g.) (Löwenbein, *loc. cit.*) was similarly pyrolysed, oily drops of 5-methyl-3-phenylcoumaran-2-one (II*c*) appeared which solidified on cooling. The solid crystallised from ethyl alcohol in colourless crystals, m. p. 106° (0·75 g., *ca.* 75%) (identity : mixed m. p. and colour reaction with sulphuric acid; *idem*, *Ber.*, 1895, **28**, 989).

(*c*) 5 : 5′-Dichloro-2 : 2′-diketo-3 : 3′-diphenyl-3 : 3′-dicoumaranyl (I*d*) (1 g.) (Arventi, *loc. cit.*) similarly afforded 5-chloro-3-phenylcoumaran-2-one (II*d*) as colourless crystals (from ethyl alcohol), m. p. 124° (0·82 g., *ca.* 82%) (identity : mixed m. p. and colour reaction with sulphuric acid; Stoermer, *Ber.*, 1911, **44**, 1863).

Reactions with phenylmagnesium bromide. (*a*) An ethereal solution of phenylmagnesium bromide [from magnesium (1·8 g.), bromobenzene (18·8 g.), and dry ether (100 c.c.)] was filtered and divided into two portions. To one portion, 2 : 2′-diketo-3 : 3′-diphenyl-3 : 3′-dicoumaranyl (I*a*) (1·5 g.) (Schönberg and Mustafa, *J.*, 1945, 657) and dry benzene (30 c.c.) were added. To the second portion, only dry benzene (30 c.c.) was added. The two portions were then refluxed for 2 hours, kept overnight at room temperature, decomposed with cold aqueous ammonium chloride, and extracted with ether. The ethereal solutions were washed with water, dried (Na_2SO_4), and evaporated. The oily residue obtained from the first portion was subjected to steam-distillation, and the aqueous distillate extracted with ether, dried, and evaporated, giving diphenyl as colourless crystals, m. p. 71° (0·7 g.) alone or mixed with an authentic specimen. The non-volatile oil solidified on cooling and crystallised from benzene–light petroleum (b. p. 30—50°) as colourless crystals, m. p. 114° (1·26 g., *ca.* 87%); it was 3-phenylcoumaran-2-one (II*a*) (mixed m. p. and colour reaction with sulphuric acid) (Found : C, 79·7; H, 4·8. Calc. for $C_{14}H_{10}O_2$: C, 80·0; H, 4·8%) (Bistrzycki and Flatau, *loc. cit.*).

The oily residue obtained from the evaporation of the second ethereal solution, similarly treated, gave only diphenyl, m. p. 71° (0·21 g.).

In a blank experiment a solution of (I*a*) (1·5 g.) in dry benzene (30 c.c.) was refluxed for 2 hours in a stream of dry carbon dioxide and kept over-night at room temperature. On concentration of the benzene solution, (I*a*) was recovered completely or almost completely unchanged (m. p. and mixed m. p.).

(*b*) 2 : 2′-Diphenylthioindigo-white (III) (Kalb and Baeyer, *Ber.*, 1913, **46**, 3879) (1·5 g.), when similarly treated, gave 2 : 3-dihydro-3-keto-2-phenylthionaphthen (IV) (1·1 g., *ca.* 75%), m. p. 105° (from ethyl alcohol) (mixed m. p. and colour reaction with sulphuric acid; Kalb and Baeyer, *loc. cit.*) (Found : C, 74·1; H, 4·0; S, 13·8. Calc. for $C_{14}H_{10}OS$: C, 74·3; H, 4·4; S, 14·1%), and diphenyl, m. p. 71° [from light petroleum (b. p. 40—60°)] (0·67 g.).

(*c*) 2 : 2′-Diketo-6 : 6′-dimethyl-3 : 3′-diphenyl-3 : 3′-dicoumaranyl (I*b*) (1·5 g.) afforded 6-methyl-3-phenylcoumaran-2-one (II*b*) (1·17 g., *ca.* 80%), m. p. 122° (from ethyl alcohol) (identity : mixed m. p. and colour reaction with sulphuric acid; Bistrzycki and Flatau, *loc. cit.*), together with diphenyl (0·64 g.).

(*d*) 2 : 2′-Diketo-5 : 5′-dimethyl-3 : 3′-diphenyl-3 : 3′-dicoumaranyl (I*c*) (1·5 g.) similarly gave 5-methyl-3-phenylcoumaran-2-one (II*c*), m. p. 106° (from ethyl alcohol) (1·1 g., *ca.* 73%) (identity : mixed m. p. and colour reaction with sulphuric acid; Bistrzycki and Flatau, *loc. cit.*), and diphenyl (0·68 g.).

(*e*) 5 : 5′-Chloro-2 : 2′-diketo-3 : 3′-diphenyl-3 : 3′-dicoumaranyl (I*d*) (1·5 g.) similarly gave 5-chloro-3-phenylcoumaran-2-one (II*d*), m. p. 124° (from ethyl alcohol) (1·13, *ca.* 76%) (identity : mixed m. p. and colour reaction with sulphuric acid; Stoermer, *loc. cit.*), and diphenyl (0·60 g.).

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The Application of Radioactive Indicators in Biochemistry.

FARADAY LECTURE, DELIVERED BEFORE THE CHEMICAL SOCIETY IN EDINBURGH ON MARCH 29th, 1950.

By PROF. G. C. HEVESY, FOR. MEM. R. S.

IT is with a feeling of deep reverence that I am delivering this lecture in commemoration of the great genius and pioneer Michael Faraday.

Throughout the century which saw the birth of Dalton's atomic theory and witnessed Faraday's fundamental discoveries, each chemical element was considered to be built up of one kind of immutable atoms. Radioactivity has completely changed this conception. As shown by Rutherford and his school, we are witnessing here the decay and birth of new atomic species, and it was soon recognized that some of these, seen from the chemist's view-point, were just new editions of well-known chemical elements. To quote a few examples, it became clear that radio-thorium was chemically practically identical with thorium, and radium-D or thorium-B with lead.

The discovery of this extraordinary chemical similarity was due to Soddy, Boltwood, and a few other great chemists, and the new phenomenon was termed " isotopy " by Soddy. Amongst the non-radioactive elements the existence of isotopes was first revealed in the case of neon by Sir J. J. Thomson's study of positive rays, and then much extended by Aston by means of his mass spectrograph. Owing to these discoveries the realm of classical chemistry was enlarged by ever-growing territories the ultimate size of which we cannot foresee. I do not venture to give even a very condensed survey of these fundamental and far-reaching advances, but shall confine myself to the discussion of the application of radioactive isotopes as indicators in biochemical studies, made possible by the above-mentioned great progress.

Radioactive isotopes were first used in the field of inorganic chemistry. The first application of this type was made at the Vienna Institute for Radium Research early in 1913 by my friend Professor Paneth, now Director of the Londonderry Laboratory of Radiochemistry in Durham, and myself. In the years to follow radioactive isotopes were applied by us, and by a small number of other workers, in various studies in the field of inorganic chemistry, and these researches proceeded at a much enhanced rate after the discovery of artificial radioactivity and the construction of the cyclotron and the uranium pile which enlarged immensely the number of radioactive isotopes available as indicators. However, radioactive tracers found their most important application in the field of biochemistry, physiology, and pathology. The intricate chemical processes taking place in the living organism, the numerous competing routes which atoms, molecules, and larger building stones follow in the plant and animal organism, open a most fertile field for the application of radioactive isotopes.

By making use of radioactive indicators we can label atoms (ions), molecules, and even larger units such as erythrocytes, leucocytes, bacteria, and viruses; subsequently, their path and fate in the living organism can be followed. I want to consider some examples of each of these three main types of body constituents, starting with a discussion of the application of radio-sodium in the study of the distribution and circulation of sodium ions.

Application of Radio-sodium in Distribution Studies.

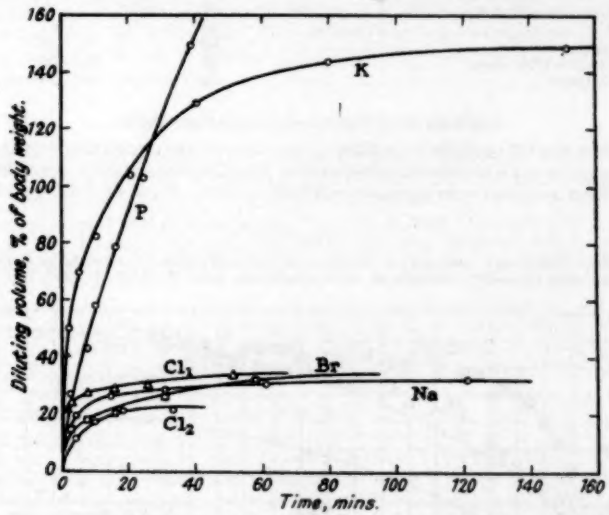
We injected sodium chloride containing some radio-sodium (^{24}Na, half-life = 14 hours) into the circulation of the rabbit. Since the sodium content of the plasma amounts to about 2 g., and the labelled sodium administered amounts to only a few micrograms, the change of the sodium content of the plasma caused by injection of labelled sodium remains within the limits of physiological variations. By introducing ^{24}Na we label, however, the circulating sodium ions. Within the errors of the experiments the radio-active ^{24}Na ions behave in the same manner as do the common ^{23}Na ions. The disappearance of 1% of the injected ^{24}Na from the blood plasma thus indicates the simultaneous disappearance of 1% of all sodium ions present in the circulation at the time of injection and their replacement by sodium ions present in the extravascular space.

When we first carried out such experiments in collaboration with Dr. Hahn, we were amazed at the velocity of disappearance of the individual sodium ions present in the circulation and at the velocity of interchange between intravascular and extravascular sodium, which involves a passage of the capillary wall. After the lapse of one minute almost ⅔ of the sodium ions present at the time of injection were no longer located in the circulation. The rate of disappearance of sodium from the circulation of the rabbit—more correctly the rate of replacement of plasma sodium by extravascular sodium—is seen in Fig. 1.[1] The time following the injection of labelled sodium, the injection taking a few seconds only, is plotted against the volume of diluting fluid necessary to reduce the ^{24}Na concentration of the plasma to the value observed.

Fig. 1 demonstrates the fundamental difference, long known to the physiologist, between the behaviour of sodium, chloride, and bromide, on the one hand, and of potassium and phosphate, on the other. Sodium and chloride ions present at the start of the experiment not only disappear rapidly from the plasma, but an exchange equilibrium between the intravascular and extravascular ions is also obtained in a short time. The same is not true for potassium and phosphate.

FIG. 1.

Rate of disappearance of various labelled ions from blood plasma of the rabbit (reproduced, with permission, from Acta Physiol. Scand., 1941, **1**, 347).



Sodium, chloride, and bromide are found mainly in the body fluid circulating outside the tissue cells, whereas potassium and phosphate appear chiefly inside the tissue cells. The intrusion of potassium or phosphate into the tissue cells requires a much longer time than the passage of the capillary wall which the " extracellular " ions alone have to perform.

Flexner and his colleagues,[2] who made extensive studies on the rate of interchange of plasma and extravascular sodium, found in the guinea-pig 60% of plasma sodium to be replaced each minute by extravascular sodium. In man, the corresponding figure was found to be 78%.* Thus, in the course of each minute, about 7 g. of sodium leave the human circulation and are replaced by sodium circulating in the extravascular fluid of the various organs. This remarkable rate of interchange is made possible by the fact that 1 ml. of blood plasma in the capillaries is exposed to an area of capillary wall of 5600 sq. cm.

By making use of radio-sodium, we can also determine the volume of the extracellular fluid

* These experiments were carried out on pregnant subjects; in normal human subjects 32% is reported (Burch, Reaser, and Cronwick, *J. Lab. Clin. Med.*, 1947, **32**, 1169).

[1] Hevesy and Hahn, *Acta Physiol. Scand.*, 1941, **1**, 347.

[2] *Cold Spring Harbor Symp. Quant. Biol.*, 1948, **13**, 88.

present in the organism,[3] a problem of great interest to the physiologist. From Fig. 1 it is seen that the extracellular volume indicated by the distribution of the injected sodium, the " sodium space," constitutes 23% of the rabbit's weight. By comparing the radio-sodium content of 1 g. of plasma water and 1 g. of fresh tissue, we find in a similar way the values for the sodium space of each organ. We can check these results by injecting into the rabbit a sodium chloride solution containing radio-chloride as an indicator.[4] In both cases very similar values are obtained for the extracellular fluid volume of most organs. The " sodium space " of the skeleton, however, was found to be more than twice as large as its " chloride space," as is seen from Table I. From this result it follows that an appreciable part of the skeleton sodium is not circulating in the cellular interspaces, but is present as an intracellular constituent of the bone tissue, possibly replacing some bone calcium in the apatite-like mineral constituents of the skeleton.

TABLE I.

Percentage extracellular water content of organs of the rabbit, calculated from the radio-sodium : radio-chloride ratio of 1 g. of fresh tissue and 1 g. of plasma water (" sodium space " and " chloride space").

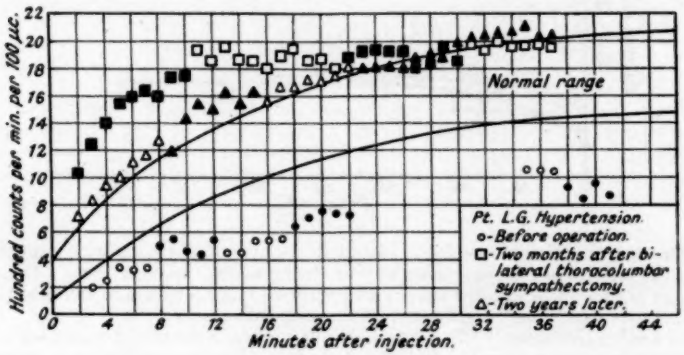
Organ.	Sodium space.	Chloride space.
Liver	22	25
Gastrocnemius muscle	10	9·4
Brain	10	11
Bone femur (dog)	66	24
Bone radius tibia (dog)	66	20
Bone humerus	63	18

Application of Sodium in Circulation Studies.

Radio-sodium can successfully be applied in the study of the circulation velocity of the body fluids. Although, in experiments described earlier, blood-plasma samples were taken at various intervals and their activites were compared with the activity of a known aliquot of the injected

FIG. 2.

Radio-sodium " build-up " curves in a patient with severe hypertension relieved by thoracolumbar sympathectomy (Quimby) (reproduced, with permission, from Nucleonics, 1947, Dec., p. 1).



sodium chloride, yet in circulation studies it may be desirable to measure outside the body the rate of propagation of the activity injected. As radio-sodium emits not only β-rays, but also penetrating γ-rays, we can very conveniently measure the time which the injected sodium takes to reach the foot by injecting radio-sodium into the arm vein and placing a Geiger counter on the foot. The average value for the circulation time is found to be 45 seconds, the values varying between 15 and 90 seconds.

We may also be interested in determining after the injection of radio-sodium into the

[3] Griffiths and Maegraith, *Nature*, 1939, **143**, 159; Kaltreiter *et al.*, *J. Exp. Med.*, 1941, **74**, 569.
[4] Manery and Bale, *Amer. J. Physiol.*, 1939, **126**, 578.

circulation the time necessary to establish equilibrium between the radio-sodium content of the plasma and that of the extracellular fluid. This time, although only a few minutes in the rabbit or guinea-pig, is appreciably longer in human subjects; it is very different in normal subjects from that in patients suffering from peripheral vascular diseases. Such determinations may thus have diagnostic value.

Quimby [5] injected radio-sodium into an anticubital vein and, by holding the window of a portable shielded Geiger counter against the sole of the foot, measured the arm-to-foot circulation As long as a uniform distribution of the injected radio-sodium in the extracellular fluid of the body is not reached, the activity of the foot increases. In individuals with no vascular disturbance this stage is reached after the lapse of 45 minutes. Curves indicating the increase in the activity of the foot with time both in the normal and in the diseased organism are shown in Fig. 2.

For patients with various vascular disorders the curves may be within, above, or below the normal region. In the curves, solid symbols represent counts against the right foot, open ones against the left foot. The chart shows data from a patient suffering from severe hypertension relieved by bilateral thoracolumbar sympathectomy. The lowest curve (circles) represents a test made before the operation. The two upper curves (squares and triangles) show the result of tests made two months and two years, respectively, after operation. They demonstrate the far-reaching change in the circulation of sodium ions produced by the operation.

Information on the effectiveness of blood flow can be obtained by measuring the rapidity of disappearance of radio-sodium following intramuscular injection of labelled sodium chloride.[6] Radio-sodium therefore proves to be an important tool in the study of circulation of body fluids, a process of basic importance.

Further Applications of Radio-sodium.

The application of radio-sodium as an indicator opens a convenient way to determine the permeability of phase boundaries of different type present in the animal and plant organisms; [7] nevertheless, it has its limitations.[8] Radio-sodium being used as a tracer, the rate was measured at which sodium passes through the placenta from the mother to the offspring, passes from the circulation into the cerebrospinal fluid, penetrates into the aqueous tumour or through the stomach wall, intrudes into the erythrocytes,[11, 12] is distributed between cytoplasm and nucleus,[9] and so on.

Time does not permit me to describe the interesting experiments of Levi and Ussing,[10] which prove that the two sides of the frog's skin have a distinctly different permeability to sodium. In these experiments the Ringer solution facing the inner surface of the excised frog skin was labelled by addition of the short-lived ^{24}Na, while the long-lived ^{22}Na was added to the Ringer solution facing the outer skin surface.

Although the terrestrial and meteoric abundance of sodium is somewhat greater than that of potassium, yet in the living organism with very few exceptions potassium is by far the more abundant element. Mammalia, for example, contain about 3 times as much potassium as sodium. As already mentioned, potassium is located mainly in the tissue cells, sodium in the extracellular body fluid. Before the application of radioactive indicators, the great difference between the sodium content of the muscle cells and the surrounding fluid, or between the red corpuscles and the surrounding plasma, for example, was interpreted as a consequence of the impermeability of the phase boundaries to sodium. The application of radio-sodium in permeability studies revealed, however, that sodium penetrates very easily from the blood plasma into the red corpuscles, and *vice versa*,[11, 12] and the same applies also to potassium.

In spite of the marked permeability of the red corpuscles to sodium and potassium, the latter element is strongly (about 30 times) concentrated in the red corpuscles, while sodium is about 10 times more abundant in the plasma than in the (human) erythrocytes. Such a difference cannot be explained without assuming a distinct difference in the chemical affinity of sodium and potassium to some type of organic cellular constituents, a difference which makes potassium a

[5] *Nucleonics*, 1947, Dec., p. 1.
[6] Elkin, Cooper, Rohrer, Miller, Shea, and Dennis, *Surg. Gynecol. Obstet.*, 1948, **87**, 1.
[7] Cf. Hevesy, "Radioactive Indicators," Interecience Publishers, New York, 1948.
[8] Ussing, *Cold Spring Harbor Symp. Quant. Biol.*, 1948, **13**, 193.
[9] Abelson and Duryee, *Biol. Bull.*, 1949, **96**, 205.
[10] *Nature*, 1949, **164**, 928.
[11] Hahn, Hevesy, and Rebbe, *Biochem. J.*, 1939, **33**, 1549.
[12] Cohn and Cohn, *Proc. Soc. Exp. Biol. Med.*, 1939, **41**, 445.

more effective competitor for the cellular ionic content than sodium. Levi and Ussing [13] brought important arguments for the view, formerly advocated by Lundegårdh [14] and by Krogh,[15] that these hypothetical organic complexes are present in the phase boundary. The red corpuscle membrane, though impermeable to sodium ions, contains scattered anions of a substance which forms a stable complex with sodium. Owing to thermal movements these complex molecules will come into contact sometimes with the outside medium and sometimes with the inside medium. If the inside solution contains ^{24}Na ions, these may exchange with ^{23}Na in some of the complex molecules, and when these molecules later touch the outside solution, ^{24}Na will leave the complex in exchange.

The application of radioactive indicators thus revealed the existence of a new type of permeability which may be denoted as interchange permeability. It exhibits some analogy to the phenomenon of self-diffusion. The diffusion process leads usually to changes in the concentration of the diffusing substrate: so does permeability. Self-diffusion leads to a molecular interchange only without any change of concentration. The same applies to interchange permeability. The individual sodium ions are soon found in the corpuscles and soon in the plasma without disturbing the prevailing concentration differences between the two phases.

Although by far most of the sodium of the organism is found in the circulating body fluid, yet it is not only a main constituent of that fluid but fulfils many important tasks besides this. This is obvious, *inter alia*, from the recent results obtained by Buchanan and his colleagues [16] in their investigations of glycogen formation in which radio-carbon was applied as indicator. When liver slices were incubated in the presence of labelled pyruvate, formation of labelled glycogen and other labelled carbohydrates was found to take place. In these experiments the addition of sodium, but not however of potassium, to the incubating medium was found to stimulate 2- and 3-fold the formation of carbohydrates other than glycogen, while addition of potassium promoted the formation of glycogen.

Labelling of Molecular Body Constituents.

Rate of Molecular Renewal.

In the study of the fate of molecular constituents, such as glycerophosphate, nucleic acid, or hæmoglobin, in the organism we frequently do not introduce into the body labelled molecules, but marked precursors of these compounds. Introduction of glycerophosphate containing radio-phosphorus into the circulation, for example, will soon be followed by an enzymatic decomposition of that compound, a small percentage only of the glycerophosphate administered reaching the liver and other organs. It is not the determination of this percentage we are mostly interested in; we wish to know primarily the rate and the main place of formation of glycerophosphate. This information we can obtain by introducing labelled inorganic phosphate, some of which rapidly reaches the liver and is incorporated into newly formed glycerophosphate molecules. By comparing the activity of 1 mg. of liver inorganic P with that of 1 mg. of liver glycerophosphate P, we arrive at a figure characterizing the rate of formation or, as the glycerophosphate content of the liver remains constant during the experiment, the rate of renewal of glycerophosphate molecules or, more correctly, for reasons stated below, the lower limit of that rate. If after the lapse of two hours 1 mg. of glycerophosphate P has an activity corresponding to $\frac{1}{16}$ of the activity of the inorganic P, we may conclude that $\frac{1}{16}$ of the glycerophosphate molecules present in the liver was renewed during two hours.[17] When carrying out such calculations we must taken into account the change with time in the activity of 1 mg. of inorganic phosphate, usually denoted as its "specific activity." The specific activity of glycerophosphate phosphorus, for example, is the percentage of administered ^{32}P present in 1 mg. of that phosphorus. It is the specific activity of the glycerophosphate P measured at the end of the experiment which has to be compared with the mean value of the specific activity of the inorganic P during the experiment. In an experiment lasting two hours the end value and the mean value of the specific activity of the inorganic P in the liver of the rat happen to be about identical. A formula which enables us to calculate for any organ and at any time the rate of turnover from data indicating the change with time of the specific activity of both the precursor and the compound considered is given by Zilversmit and his associates.[18]

[13] *Acta Physiol. Scand.*, 1948, **16**, 232.
[14] *Protoplasma*, 1941, **35**, 548.
[15] *Proc. Roy. Soc.*, 1946, *B*, **133**, 140
[16] Buchanan, Hastings, and Neslett, *J. Biol. Chem.*, 1949, **180**, 435, 447.
[17] Hevesy and Hahn, *Kgl. Danske Videnskab. Selsk. Biol. Medd.*, 1940, **15**, Nr. 5.
[18] Zilversmit, Entenmann, and Fishler, *J. Gen. Physiol.*, 1943, **26**, 325.

The greatest difficulty we encounter when determining the renewal rates of molecular body constituents is often the lack of knowledge of the pertinent precursor of the compound. We can probably assume inorganic P to be the pertinent precursor of glycerophosphate P. In the case of lecithin, however, the labelled inorganic P may, before its incorporation into the lecithin molecules, have to be converted into glycerophosphate P or another intermediary compound. If the formation of glycerophosphate takes an appreciable time, in the first phase of the experiment, then after administration of labelled inorganic phosphate, the newly formed lecithin molecules do not become labelled as they were synthesized with the participation of yet inactive glycerophosphate molecules. When calculating the renewal rate of glycerophosphate by comparing the specific activities of the liver inorganic P and liver lecithin P we thus underestimate the turnover rate of lecithin. This would not be the case if we compared the specific activities of the glycerophosphate P and the lecithin P of the liver.

In the liver of the dog, for example, the half-life of the lecithin molecules was calculated, inorganic P being assumed to be the pertinent precursor, to be 12·5 hours, while with the assumption that glycerophosphate P is incorporated into the lecithin molecule, the much lower value of 3·6 hours was obtained.[19] These figures indicate the half-life of the average lecithin molecule of the liver. When, however, investigating the renewal rate of lecithin present in different cellular fractions of the liver, pronounced differences are found. As seen in Table II, the rate of renewal of the phosphatide molecules present in the cell nuclei, and to a minor extent also those present in the mitochondria, is markedly lower than the corresponding figure for the average tissue phosphatides. The figures were obtained two hours after injection of labelled phosphate.[20]

TABLE II.

Renewal rate of phosphatide P *of the liver fractions of the rat.*

Phosphatide fraction.	Activity of 1 mg. of phosphatide P in percentage of the activity of 1 mg. of :		
	Plasma phosphate.	Liver phosphate.	Liver glycerophosphate.
Total tissue	13·4	12·8	18·8
Mitochondria	9·4	9·0	13·1
Cell nuclei	5·6	5·4	7·9

Ample evidence is available to support the assumption that the incorporation of labelled phosphate into phosphatide or other organic phosphorus compounds involves enzymic processes, no " physical " interchange taking place. In the study of phosphatides in surviving liver slices incubated in a Ringer solution containing labelled phosphate, for example, the formation of " marked " phosphatides takes place under aerobic conditions only.[21] Absence of oxygen or presence of respiratory inhibitors should clearly not interfere with a non-enzymic type of interchange.

It was the introduction of the method of isotopic indicators which has drawn the attention to the notion of the lifetime of the molecules building up the organism, a magnitude formerly not considered. The first lifetime determination, performed almost immediately after the discovery of deuterium, was that of the water molecules of the goldfish.[22] The water molecules present in the *living* goldfish were found to interchange rapidly with those of the surrounding water, and some of the hydrogen atoms (the " labile " hydrogen) of the organic tissue components were found to be replaced at a remarkable rate by the hydrogen atoms of the body water.

Shortly afterwards, the lifetime of the water molecules present in the human body was measured.[22a] Dilute heavy water being used as an indicator, following the intake of a known volume of dilute (2%) heavy water, the heavy-water content of the urine was determined; from these and other excretion figures the average lifetime of water molecules in a test person was found to be 14 days. This value clearly depends not only on the total water content but also on the water intake of the subject.

In the same investigation the total water content was calculated from the heavy-water content of the water drunk and that of the body water after exchange equilibrium between the water molecules taken in and those already present in the organism was reached. The heavy-water content of the body water was obtained by determining the heavy-water content of urine

[19] Zilversmit, Entenmann, and Chaikoff, *J. Biol. Chem.*, 1948, **176**, 193; Popják and Muir, *Biochem. J.*, 1950, **46**, 103.
[20] de Elliott and Hevesy, *Acta Physiol. Scand.*, 1950, **19**, 370; cf. Ada, *Biochem. J.*, 1949, **45**, 422.
[21] Taurog, Chaikoff, and Perlman, *J. Biol. Chem.*, 1942, **145**, 281.
[22] Hevesy and Hofer, *Z. physiol. Chem.*, 1933, **225**, 28.
[22a] *Idem*, *Nature*, 1934, **134**, 879.

water. The total water content of the test person was found to form 64% of the body weight. For abnormally adipose individuals figures as low as 40%, for lean ones as high as 70%, have recently been obtained.[23]

The interest of the biochemist in the lifetime of the molecules building up the organism was soon much enhanced by the classical work of Schoenheimer and Rittenberg,[24] who determined first the lifetime of fat molecules and later many other types of molecules in the animal body and, moreover, by the investigation of radio-phosphorus in similar investigations, the first of which was the renewal rate of the mineral constituents of the bone.[25]

Place of Formation of Molecular Constituents.

Having discussed the rate of renewal of phosphatide molecules, I want now to say a few words about the place of formation of phosphatide molecules in the yolk of the hen's egg and in the blood plasma. The determination of the place of formation of body constituents is another important field of application for isotopic indicators.

Only a few hours after administration of labelled phosphate to the hen, the presence of radioactive lecithin and other phosphatides can be detected in the yolks of the ovary. These phosphatide molecules may have been synthesized in the yolk or carried into the yolk by the circulating plasma, an alternative explanation being the incorporation into the yolk of phosphatide molecules built up in the ovary. Now, it can be shown by experiments *in vitro* that penetration of labelled phosphates into the egg followed by intrusion into the yolk does not lead to the formation of labelled phosphatide molecules.[26]

In view of the fact that the specific activity of the phosphatides of the ovary is lower than that of the yolk phosphatides, as seen in Table III, the former cannot be the source of the latter.[26]

TABLE III.

Specific activity of phosphatide P *in organs of the hen.*

Organ.	Relative specific activity.
Liver	100
Plasma	79
Ovary	7·2
Yolk	9·2
Intestinal mucosa	18

The specific activity of the precursor of a product obviously cannot be lower than that of the product itself, at least at that phase of the experiment in which the specific activity of the precursor increases with time. Thus we have to conclude that the yolk phosphatides originate from the plasma phosphatides. The source of the plasma phosphatides, or at least their main source, must be the liver phosphatides as alone the liver phosphatides have a higher specific activity than the plasma phosphatides. Even the specific activity of the phosphatides of the intestinal mucosa in which phosphatides are turned over at a remarkable rate as seen in Table III is lower than that of the plasma phosphatides.

While the plasma phosphatides contain mainly lecithin, appreciable amounts of cephalin are also present in the liver. In view of the small differences in the turnover rate of lecithin and cephalin in the liver, the difference in the composition of liver and plasma phosphatides does not influence the above conclusion.

The most direct approach to the solution of the problem of the origin of plasma phosphatides is a comparison of the specific activity of plasma phosphatides in the intact and in the hepatectomized animal. In their experiments Fishler *et al.*[27] found that, after the administration of labelled phosphate in contrast to the phosphatides of the plasma of the intact dog, the plasma phosphatides of the liver-less dog contained only a negligible amount of ^{32}P. As in both cases the same amount of labelled phosphate was administered to the dog, this result fully confirms the above conclusion that the liver is almost the sole place of formation of plasma phosphatides.[28]

[23] Drabkin, *Fed. Proc.*, 1950, **9**, 182.
[24] *J. Biol. Chem.*, 1935, **111**, 175; Schoenheimer, "The Dynamic State of Body Constituents," Cambridge, Mass., 1942.
[25] Chievitz and Hevesy, *Nature*, 1935, **136**, 753.
[26] Hevesy and Hahn, *Kgl. Danske Videnskab. Selsk. Biol. Medd.*, 1938, **14**, Nr. 2.
[27] Fishler, Entenmann, Montgomery, and Chaikoff, *J. Biol. Chem.*, 1943, **150**, 47; Entenman, Chaikoff, and Zilversmit, *ibid.*, 1946, **166**, 15.
[28] Cf. also Popják and Beeckmans, *Biochem. J.*, 1950, **46**, 99.

The above-mentioned lack of extra-ovarian formation of labelled phosphatide in the yolk is also brought out in experiments with incubated fertilized eggs into which labelled phosphate was injected.[29] While the fœtal phosphatides present in such eggs have a high ^{32}P content, the remainders of the yolk still present in such eggs do not contain significant amounts of labelled phosphatides, as seen in Table IV. The slight activity of yolk phosphatides, which increases with age of the embryo, is possibly caused by influx from the embryo into the yolk of a small amount of labelled phosphatides or of the enzymes responsible for resynthesis of phosphatides.

TABLE IV.

Specific activity of phosphatides extracted from embryo and residual yolk of the hen's egg.

Time of incubation days.	Phosphatides extracted.	Specific activity.
6	Yolk	0·032
	Embryo	100
11	Yolk	0·10
	Embryo	100
18	Yolk	0·92
	Embryo	100

Similar considerations were applied by Aten[30] to the study of the origin of the milk phosphatides in the goat. Table V demonstrates that at least most of the phosphatide molecules of the milk are not those which passed from the blood plasma into the milk, but those which had their origin in the milk gland, the phosphatides of the milk being much more active than those of the plasma, but less active than those of the milk gland.

TABLE V.

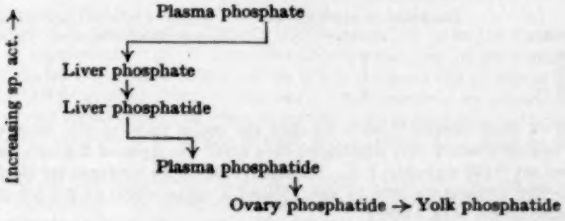
Activity of phosphatide phosphorus of milk and organs of a goat.[30]

Organ.	Specific activity.	Organ.	Specific activity.
Milk	1	Liver	1
Plasma	0·02	Kidneys	1·2
Milk gland	1·4		

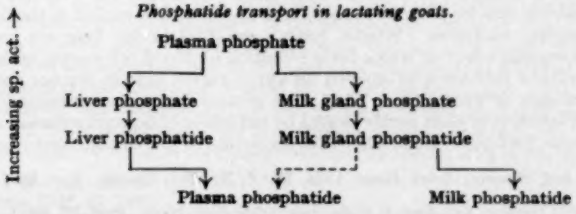
The following scheme represents the course of phosphatide transport in laying hens and in lactating goats.[30]

Scheme for the specific activity of phosphatides.[30]

Phosphatide transport in laying hens.



Phosphatide transport in lactating goats.



[29] Hevesy, Levi, and Rebbe, *ibid.*, 1938, **32**, 2147.
[30] Aten, "Isotopes and Formation of Milk and Egg," 1939, Diss., Utrecht; Aten and Hevesy, *Nature*, 1938, **142**, 111.

Effect of Irradiation with X-Rays on the Formation of Nucleic Acids.

The application of radioactive indicators proved to be an efficient tool for the measurement of the change in the rate of formation of molecular body constituents caused by administration of chemicals inducing such interference or by irradiation with ionizing radiation which produces such interfering chemicals *in situ*. Such radiation may diminish the growth rate, and we can expect that it might interfere with the rate of formation of some cellular constituents already in the early or earliest phase of the experiment and with that of deoxyribonucleic acid, a main constituent of the cell nucleus.

In a growing tumour, growth, and correspondingly, additional formation of deoxyribonucleic acid, may amount to about 1% in the course of 2 hours. If this formation is supressed by irradiation, the irradiated tumour after the lapse of 2 hours can be expected to contain 1% less deoxyribonucleic acid than do the controls. The distinction between 100 and 99 deoxyribonucleic acid molecules present in a tumour by means of chemical analyses is a most difficult task. However, when applying radioactive indicators such a difference can easily be measured. Radioactive indicators permit us to distinguish between old and new molecules, between those present before the start of the experiment and those formed afterwards. The old molecules are not radioactive, but the new ones contain ^{32}P.

Let us assume that out of 100 deoxyribonucleic acid molecules present in the non-irradiated tumour two are found to contain ^{32}P two hours after administration of labelled phosphate while in the irradiated tumour, in which deoxyribonucleic acid formation is suppressed, the corresponding figure is only 1. Such a difference is readily ascertained. In the first case, the Geiger counter or another suitable measuring instrument will indicate an activity of, say, 200 counts per minute, in the second case only 100. Radioactive measurements can very easily be made, a fact which contributes materially to the wide application of the method of radioactive indicators.

In Table VI the effect of irradiation with *X*-ray doses ranging from 335 to 1500 r. on the Jensen sarcoma of the rat is shown.[30a] A few minutes after the irradiation, labelled sodium phosphate was injected into 28 rats and into the same number of controls. The effect of irradiation on the formation of deoxyribonucleic acid molecules is seen to be most effective shortly after irradiation.

TABLE VI.

Effect of X-*rays on the formation of labelled deoxyribonucleic acid after administration of labelled sodium phosphate.*

Dose, in r. units.	Duration of experiment, hours.	Ratio of labelled nucleic acid formation in non-irradiated and irradiated sarcoma.
750—1500	½	3·2
350—1500	1	2·4
650—1500	2	2·2

In another set of experiments [31] with 32 rats the mean ratio of the labelled nucleic acid formation in the non-irradiated and irradiated rats after the lapse of 2 hours was found to be 2·05, and in a third set [32] (40 animals) 2·2. Similar results were obtained by Barbara Holmes,[33] who, injecting labelled phosphate into 14 rats, found a mean value of 2·1 for the above ratio ½—2 hours after irradiation with 2·000 r.

In organs such as liver, kidney, spleen, and intestinal mucosa, the formation of deoxyribonucleic acid formation was found to be reduced to a similar extent to that in the tumour [34] under the effect of ionizing radiation. Hardin Jones's results [35] in this field are instructive. He compared the depressing effect of whole-body radiation on blood-cell counts with the reduction in the turnover rate of formation of labelled deoxyribonucleic acid in tumour and liver. Some of his results are seen in Table VII. They show similar figures for percentage depression of blood corpuscles, which is at least partly caused by inhibition of deoxyribonucleic acid formation in the bone marrow, and deoxyribonucleic acid formation in the tumour and liver.

[30a] Von Euler and Hevesy, *Arkiv Kemi*, 1944, **17**, *A*, Nr. 30; Hevesy, *Rev. Mod. Physics*, 1950, **17**, 102.
[31] Von Euler and Hevesy, *Kgl. Danske Videnskab. Selsk. Biol. Medd.*, 1942, **17**, Nr. 8.
[32] Ahlström, v. Euler, and Hevesy, *Arkiv Kemi*, 1945, **19**, *A*, Nr. 13.
[33] *Brit. J. Rad.*, 1947, **20**, 45; 1949, **22**, 487.
[34] Ahlström, v. Euler, and Hevesy, *Arkiv Kemi*, 1944, **19**, *A*, Nr. 9.
[35] Proc. Oberlin College Radiation Biology Meeting, in the press.

TABLE VII.

Depressing effect of irradiation with a dose of 1 *r. of* X-*rays* (Hardin Jones).

System investigated.	Percentage depression due to irradiation.
White corpuscle count or lymphocyte count	0·23
Red corpuscle count	0·3
Formation of labelled deoxyribonucleic acid in tumour ...	0·18
Formation of labelled deoxyribonucleic acid in liver	0·28

Indirect Radiation Effects.

The work of Dale [36] and others on the effect of *X*-rays on enzyme suspensions led to the result that part of the effect of irradiation on enzymes is caused by the production of noxious agents in the solvent. Inactivation of the enzymes is to a large extent caused by the interaction of these noxious agents produced in the water with the enzyme. Dale found that with a given dose inactivation is obtained of a considerably smaller fraction of a concentrated than of a dilute carboxy-peptidase solution. This observation suggests the explanation, and the only feasible one, that the number of inactivating atoms or molecules produced under the effect of weak doses of *X*-rays in the solvent suffices only to inactivate a restricted number of enzyme particles. The primary process in the action of radiation on water is detachment of an electron and its subsequent transfer from the ion to one of the neighbouring molecules or ions.[37] For pure water the primary process is $(HO)^-H^+ + \text{radiation} \rightleftarrows HO + H$.

Most of these decomposition products have an exceedingly short life and may recombine to form water or react with protective molecules present before they reach the enzyme surface. Besides the existence of this indirect radiation effect due to more or less short-lived radicals, the application of labelled phosphate in radiation studies revealed the existence of another type of indirect effect [38] due to a radiation product of an appreciably long life.

In animals bearing two distant tumours, one of which was irradiated while the other was effectively shielded with lead, incorporation of ^{32}P into the deoxyribonucleic acid of not only the irradiated but also the shielded sarcoma was observed. Irradiation with a dose of 280—2000 r. had an effect on the deoxyribonucleic acid formation of the shielded tumour which lagged behind with only 20—40% of that observed in the irradiated sarcoma.

Kelly and Hardin Jones [39] extended these studies and found that even local irradiation of the liver of the rat with a dose of 170 r. leads to a 34% reduction of labelled deoxyribonucleic acid formation in the tumour, while local irradiation of the muscles with 230 r. reduces the labelled deoxyribonucleic acid formation in the liver by 26%.

On introduction of the blood of a strongly irradiated rabbit into the circulation of another rabbit, the rate of incorporation of ^{32}P into deoxyribonucleic acid of the kidneys of the second rabbit was found to be reduced, an observation which suggests the presence of a substance in the circulation of the irradiated rabbit which has a blocking effect on nucleic acid formation.[40] In view of more recent results obtained when using ^{14}C as an indicator in radiation studies, which I shall discuss later, such indirect effects appear less puzzling now than at the time of their observation.

The availability of the long-lived (half-life = 5700 years) ^{14}C for tracer research was an event of great importance. It immensely increased the stimulus already provided by the applicability of the short-lived ^{11}C (half-life = 20 minutes) and the stable ^{13}C. To mention only a single example, it elucidated to a remarkable extent many steps involved in glycogen synthesis. ^{14}C was also applied in the study of the biochemical effects of *X*-rays. Into a great number of rapidly growing rats, ^{14}C incorporated with the carboxyl group of sodium acetate was injected. Before the injection, half of the rats were irradiated with a dose of 900 r. The silver purines of deoxyribonucleic acid isolated from some of the organs were then obtained, and their radioactivity was compared.[41] On irradiating new-born mice with about 900 r., the incorporation of ^{14}C into the purines of the deoxyribonucleic acid was found to be depressed to an extent similar to that of ^{32}P incorporation into deoxyribonucleic acid in the above-mentioned

[36] *Biochem. J.*, 1940, **34**, 1367.
[37] Weiss, *Nature*, 1944, **53**, 748.
[38] Ahlström, v. Euler, and Hevesy, *Arkiv Kemi*, 1945, **19**, *A*, Nr. 13; Holmes, *Brit. J. Radiol.*, 1949, **22**, 487.
[39] *Proc. Soc. Exp. Biol. Med.*, 1950, **74**, 493.
[40] Ahlström, v. Euler, Hevesy, and K. Zerahn, *Arkiv Kemi*, 1946, **23**, *A*, Nr. 11.
[41] Hevesy, *Nature*, 1949, **163**, 869.

experiments. Furthermore, experiments carried out in Chicago * brought out a depressing effect of irradiation on the incorporation of ^{14}C into the purines of ribonucleic acid similar to that observed in the case of the deoxyribo-compound. The incorporation of ^{32}P into ribonucleic acid [33] was found, however, to be markedly less susceptible to the effect of irradiation than its incorporation into the deoxy-compound.

Renewal of Ribonucleic Acid.

A very appreciable part of the incorporation of ^{32}P into ribonucleic acid molecules may be due to rephosphorylation of such molecules. If, in contrast to the synthesis of the total molecule the rephosphorylation process is not radiosensitive, we may find an explanation in the difference of the effect of radiation on the incorporation of ^{32}P and ^{14}C into the ribonucleic acid molecules. This explanation is very hypothetical, and I mention it mainly because it offers a welcome opportunity to emphasize the fact that isotopic tracers may indicate fundamentally different processes, such as renewal of one of the molecular constituents only or synthesis of the whole molecule from primitive precursors and, furthermore, intermediates between these two extreme cases.

Let us consider a compound such as adenosine triphosphoric acid. This molecule contains two labile, easily removed phosphate groups, and a third one incorporated into the adenylic acid moiety. In the animal organism, intrusion of the administered labelled inorganic phosphate into tissue cells is followed by a strikingly rapid interchange between the labelled phosphate ions and the labile phosphate groups of the adenosine triphosphoric acid. An interchange may even take place during the passage of the labelled inorganic phosphate through the boundary of the intra- and extra-cellular spaces, as pointed out by Sachs.[41] The adenylic acid moiety is not involved in this very rapid renewal process. The rate of incorporation of ^{32}P into the adenosine triphosphate is thus a measure of the rate of rephosphorylation only of that molecule and not of its formation from early precursors. Even in a rapidly growing mammalian organ, in which the adenosine triphosphoric acid content may increase by as much as 1% per hour, such an increase involving 1% additional formation of adenosine triphosphoric acid from early precursors, the incorporation of ^{32}P is negligible compared to incorporation of ^{32}P by rephosphorylation.

Incorporation of ^{32}P into deoxyribonucleic acid of a growing organ, *e.g.*, a tumour, is of a very different type. Even if some rephosphorylation in such molecules cannot be excluded, the incorporation of ^{32}P into deoxyribonucleic acid of a growing organ takes place mainly in the course of mitotic processes in which necessarily the whole molecule is involved. This appears from the parallelism often found between the mitotic figure and the rate of ^{32}P incorporation into deoxyribonucleic acid of the organ. In organs in which appreciable cell division takes place, such as in the bone marrow, the thymus gland, the intestinal mucosa, or the spleen, administration of labelled phosphate to the rat is promptly followed by a remarkable formation of labelled deoxyribonucleic acid molecules. This is not the case in the liver or kidney of the fully-grown animal in contrast to the corresponding organs of the newly-born rat. We shall see later, when discussing the life-cycle determination of blood corpuscles, that the deoxyribonucleic acid phosphorus of the circulating avian red corpuscle and of the mammalian white corpuscle in which mitotic processes do not occur is entirely stable during the lifetime of such particles, and that incorporation of ^{32}P into the deoxyribonucleic acid of such particles takes place only during their formation.

The Jensen sarcoma of the rat grows by about 1% per hour, and its deoxyribonucleic acid content increases correspondingly by about 1%. When calculating the growth rate from ^{32}P data, assuming inorganic ^{32}P to be the pertinent precursor of deoxyribonucleic acid ^{32}P and also the absence of all rephosphorylation of the deoxyribonucleic acid molecules, we arrive at about twice the above value.

When calculating the formation rate of deoxyribonucleic acid molecules from ^{32}P data, we assume that the pertinent precursor of deoxyribonucleic acid P is the intracellular inorganic P or labile adenosine triphosphate P, and compare the value of the specific activity of deoxyribonucleic acid P at the end of a 2-hour experiment with the mean value of the specific activity of inorganic P during the experiment. If the incorporation of phosphate into a deoxyribonucleic acid molecule was preceded by a comparatively much slower formation of a phosphate-containing precursor, for example of phosphorylated sugar, the above method of calculation would not be

* Personal communication by Dr. Guzman Barron.

[41] *Cold Spring Harbor Symp. Quant. Biol.*, 1948, **13**, 180.

justified. We should then compare the specific activity of the P of the hypothetical precursor with that of the P of deoxyribonucleic acid. Ottesen, however (cf. p. 1631), succeeded in showing that in the case of the avian red corpuscles the existence of such a precursor is incompatible with the results obtained in his life-cycle determination.

In the Jensen sarcoma the probability of the incorporation of a ^{32}P atom into a ribonucleic acid molecule was found to be 2—3 times higher than that of its incorporation into a deoxyribonucleic acid molecule.[43] As during the 2-hour experiment the percentage additional formation of ribonucleic acid in the growing tumour cannot differ much from that of deoxyribonucleic acid, the above figures indicate that out of three ^{32}P atoms at least 1—2 are incorporated into ribonucleic acid by a process which does not involve synthesis of ribonucleic acid molecules from early precursors.

I have here discussed the effect of irradiation on nucleic acid formation, as the application of radioactive indicators in the study of biological radiation effects is a good example of the usefulness of the possibility of distinguishing between " old " and " new " molecules. Since only the deoxyribonucleic acid molecules formed during the experiment, and therefore a minor percentage of those present, contain ^{32}P or ^{14}C, we can, from the fact that irradiation with ionizing radiation depresses ^{32}P or ^{14}C incorporation with such molecules, conclude that a main effect of restricted doses of irradiation as far as cell division is concerned is the obstruction of the *formation* of nucleic acid which is presumably caused by inactivation of enzymes involved in the synthesis of these compounds. A chemical analysis could only disclose changes in the deoxyribonucleic acid content, leaving the question open how far these changes are caused by enhanced degradation or obstructed formation.

In experiments in which the effect of irradiation on the incorporation of ^{14}C into the deoxyribonucleic acid was studied, acetate labelled with ^{14}C in the carboxyl group was injected into mice. In Table VIII, in addition to the effect of irradiation on ^{14}C incorporation into purine carbon of deoxyribonucleic acid, the corresponding effect on ^{14}C incorporation into protein of the liver is seen as well. Whereas incorporation into purines is markedly depressed, that into proteins is enhanced under the effect of irradiation. It is not probable that irradiation promotes protein formation. Correspondingly, the enhanced ^{14}C incorporation is interpreted as the consequence of a change in the sensitivity of the ^{14}C indicator, a change in the activity level of the protein precursor or precursors by irradiation. The activity level being higher, more ^{14}C but no more, possibly even less, protein ^{12}C is turned over. Sensitivity of the indicator plays a very important part in the application of isotopic tracers and this fact will now be considered.

TABLE VIII.

Effect of irradiation with an X*-ray dose of* 880 *r. on the incorporation of* ^{14}C *into deoxyribonucleic acid purines and into tissue proteins prepared from the livers of* 55 *new-born fed rats (mean values).*

Fraction.	Percentage change in the incorporation of ^{14}C due to the effect of irradiation.
Purines	−44
Proteins	+27

Change of Sensitivity of the Radioactive Indicator in the Course of the Experiment.

When applying isotopic indicators in the study of animal metabolism, two main lines of technique can be followed. We can keep the tracer in the body at a constant level. Deuterium for example, being used as an indicator, dilute heavy water is given to the animal throughout an experiment taking days or weeks. The body fluids soon reach a constant heavy-water content and, by comparing the deuterium content of the body water with that of fatty acids extracted from an organ, we can state what percentage of the fatty acid deuterium of that organ reached the body-water deuterium level and thus find the percentage fatty acid renewal during the experiment or, more correctly, the lower limit of that percentage. This method was much applied by Schoenheimer and Rittenberg in their classical experiments and also by Stetten, Bloch, Bernhard, and others, who obtained important information.[51]

When studying acetate metabolism, acetate labelled, for example, in the carboxyl group with ^{13}C or ^{14}C can be added to the daily food and an almost constant ^{13}C or ^{14}C content of the acetate of the body fluid will thus be obtained. As shown by Rittenberg and Bloch, and also by others,[43a] here again a comparison of the ^{13}C or ^{14}C content of the ingested acetate with that of fatty acid or cholesterol, etc., yields the lower limit of percentage renewal of these compounds.

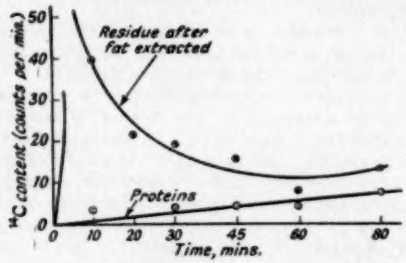
[43] Von Euler, Hevesy, and Solodkowska, *Arkiv Kemi*, 1948, **26**, *A*, Nr. 4.
[43a] Rittenberg and Bloch, *J. Biol. Chem.*, 1946, **160**, 417; Pihl, Bloch, and Anker, *ibid.*, 1950, **183**, 441.

In the work with radioactive indicators we mostly choose, however, a different technique. We administer the labelled precursor at the start of the experiment only, so the specific activity of the indicator decreases with time. On injection of labelled phosphate of negligible weight, having an activity of 1 mc., into the circulation of a human subject containing 130 mg. of plasma inorganic P this mc. will first indicate the presence of 130 mg. of inorganic phosphorus. Soon, however, as the ^{32}P of the plasma inorganic P rapidly passes the capillary wall, it interchanges with the extra-vascular inorganic ^{31}P. Owing to these and other interchanges, the ^{32}P content of the blood plasma rapidly decreases. After the lapse of 60 minutes, the ^{32}P content is reduced to about one-tenth of its original value, the presence of 130 mg. of inorganic P in the blood plasma being now indicated by an activity of 0·1 mc. only. This sensitivity of the radioactive indicator is thus increased to 10 times its initial value. A similar behaviour is shown by many other radioactive indicators.

The sensitivity of acetate ^{14}C as an indicator of body acetate increases at a remarkable rate, as seen in Fig. 3.[66] In this figure are plotted the results of experiments in which groups of mice were killed at different times after interperitoneal injection of acetate labelled in the carboxyl group with ^{14}C. The radioactivity of the fat-free brain tissue and also that of the proteins of the brain was then determined, and the figures obtained plotted against time. After only

FIG. 3.

Change with time in the ^{14}C content of brain fractions of mice after intraperitoneal injection of labelled acetate (reproduced, with permission, from Arch. internat. Pharm. Therap., 1951, **86**, 33).



30 minutes, the activity of the fat-free (acid-soluble + protein) fractions is less than half of the value observed after 10 minutes, the protein fractions showing a slow increase in their ^{14}C content with time.

The change of sensitivity of the radioactive indicator with time may be disturbing and can make the interpretation of the results obtained very difficult. On the other hand, it may also have great advantages. We shall describe some examples showing both disadvantages and advantages which result from the marked time-dependency of the sensitivity of radioactive indicators.

Renewal of the Mineral Constituents of the Skeleton.

The great inconvenience inherent in the change of the sensitivity of radioactive indicators with time becomes clear from an attempt to determine the rate of renewal of the mineral constituents of the skeleton by making use of radio-phosphorus.[44] Here we refer to the first turnover studies of body constituents with the help of a radioactive tracer, which were carried out simultaneously with the above-mentioned first investigations by Schoenheimer and Rittenberg, who used deuterium as an indicator.

Blood-plasma phosphate was found to interchange very rapidly with the uppermost phosphate layer of the apatite-like cystallites. This rapid interchange is followed by a much slower one due to a slow recrystallization of the apatite crystals. Some molecular layers go into solution while others are formed with the participation of labelled phosphate. Such layers will be comparatively strongly active in the early phase of the experiment. Owing to the decrease in the ^{32}P content of the plasma and lymph with time, they will be much less active in later phases.

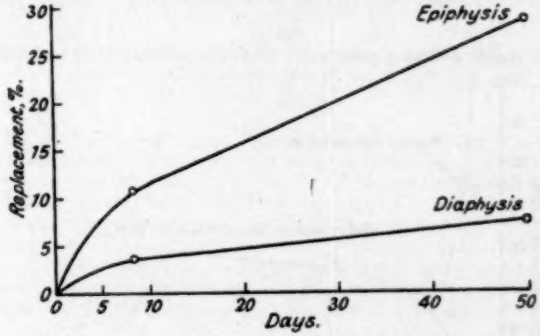
On top of a strongly active layer, slightly active layers may be deposited, protecting the first layer from dissolution. The great complexity of ^{32}P distribution in the skeleton apatite

[44] Chievitz and Hevesy, *Nature*, 1935, **136**, 754.

frustrates, or at least makes extremely difficult, a quantitative determination of the extent of renewal of the mineral constituents of the bone when labelled phosphate is administered only at the start of the experiment. We arrive at such a result when administering daily repetitions of labelled phosphate, thus keeping the level of plasma activity constant. By applying this technique, which is much less convenient, and by comparing the specific activities of the bone inorganic P and plasma inorganic P at the end of the experiment, we obtain a figure indicating the percentage of the renewed skeleton. Results obtained with rabbits, seen in Fig. 4, show that after the lapse of 50 days 74% of the soft bones (epiphysis) and as much as 93% of the hard bones (diaphysis) remained unchanged.[45] No similar experiments were carried out with human subjects but, as the extent of renewal increases only slightly with increasing time, we seem to be justified in concluding that a large part of the mineral constituents of the adult skeleton remains unchanged during life.

FIG. 4.

Extent of replacement of rabbit's bone phosphorus by labelled phosphorus (reproduced, with permission, from Biochem. J., 1940, **34**, 532).



The above-mentioned protection of highly active phosphate apatite layers by slightly active ones much resembles the protection of lead incorporated with the skeleton. From a blood plasma with comparatively high lead content, lead-replacing calcium ions are incorporated with an apatite layer. Since the lead content of the plasma decreases with time, the above-mentioned layer may be covered by others containing only negligible amounts of lead. The probability of an escape of lead from the skeleton is thus strongly reduced. It takes place, however, to some extent over long time intervals, constantly supplying the plasma with toxic lead. Not only lead but also numerous other elements, *e.g.*, uranium,[46] find more or less permanent abode in the skeleton.

Determination of the Life-cycle of Blood Corpuscles.

In the determination of the lifetime of blood corpuscles, the marked decline of the specific activity of the precursor with time proves to be most advantageous, as shown, for example, in Ottesen's work [46a] on the life-cycle of nucleated red corpuscles. After administration of labelled phosphate, the specific activity of the inorganic phosphate of the blood plasma declines, as seen in Fig. 5. It takes some time for the inorganic phosphate of the marrow to come into exchange equilibrium with the inorganic phosphate of the plasma, but after that, the specific activity of the marrow inorganic phosphate will markedly decrease with time as well. Thus, the deoxyribonucleic acid molecules formed with participation of labelled inorganic phosphate in the course of the first day are much more active than those formed later. The deoxyribonucleic acid-containing red corpuscles have a definite lifetime. As soon as this is reached they are destroyed and their nucleic acid phosphorus, which is now exposed to the effect of phosphatase, is split off and soon lost in the larger pool of inorganic phosphate present in the body. The end of the life-cycle of the red corpuscles will thus be indicated by a sudden decrease in the activity of the deoxyribonucleic acid extracted from the erythrocytes.

[45] Hevesy, Levi, and Rebbe, *Biochem. J.*, 1940, **34**, 532.
[46] Neuman and Neuman, *J. Biol. Chem.*, 1948, **174**, 711.
[46a] *Nature*, 1948, **162**, 730; Diss., Copenhagen, 1951.

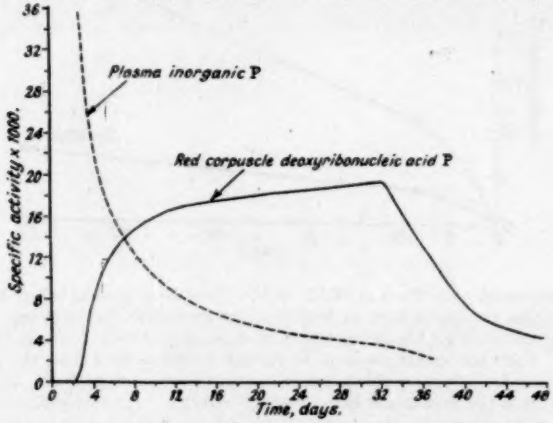
(a) *Life-time of the Avian Red Corpuscles.*—In the determination of the life-cycle of avian red corpuscles, erythrocyte samples are secured daily after injection of labelled sodium phosphate (about 15 μc.) to the hen, and the radioaticvity of their deoxyribonucleic acid P is determined. The specific activity of the plasma inorganic P is determined as well. In Fig. 5 the broken line indicates the change of the specific activity of plasma inorganic P with time, and the full line shows the corresponding values of deoxyribonucleic acid P.

The radioactivity of the deoxyribonucleic acid P of the red corpuscles formed during the first day constitutes a very large part of the radioactivity of the deoxyribonucleic acid of the total red corpuscle content of the circulation. Correspondingly, as soon as the life-cycle of the red corpuscles formed during the first day after injection of labelled sodium phosphate is accomplished, the activity of the deoxyribonucleic acid P of the total corpuscles rapidly declines, as seen in Fig. 5. The date of this rapid decline indicates almost precisely the life-cycle of the avian red corpuscles.

To arrive at a correct value of the life-cycle of the deoxyribonucleic acid, the contribution of red corpuscles formed in a later part of the experiment to the activity of the total erythrocyte deoxyribonucleic acid must be taken into account as well. This can be done by making use

FIG. 5.

Change of the specific activity of phosphorus fractions of the hen's blood with time (Ottesen).



of the following consideration. The formation of labelled deoxyribonucleic acid during the first day takes place with participation of inorganic P the specific activity of which corresponds to the mean value of the inorganic P during that time interval. This mean value, which can be experimentally determined, is denoted by $f(\frac{1}{2})$. The contribution of active deoxyribonucleic acid of red corpuscles formed during the first day of the experiment to the total activity of erythrocyte deoxyribonucleic acid measured after the lapse of 1 day is $f(\frac{1}{2})$ $(\phi\frac{1}{2})$, where ϕ is a function of the time taken by the transition of the red corpuscles from the marrow into the circulation, and also of the duration of the life-cycle of the erythrocytes. Actually, we compare, not the deoxyribonucleic acid activities of the total erythrocyte content of the circulation, but the specific activities of deoxyribonucleic acid P fractions.

The second day, the corpuscle deoxyribonucleic acid is formed from inorganic P having a much lower specific activity than the first day, the mean value of which is now $f(1\frac{1}{2})$. The contribution of active deoxyribonucleic acid formed during the second day to the total doxyribonucleic acid activity measured on the second day is now $f(1\frac{1}{2})(\phi\frac{1}{2})$. The share of the active deoxyribonucleic acid formed in the course of the first day in the total activity of deoxyribonucleic acid of the red corpuscles is somewhat different from the corresponding value during the first day and amounts to $f(\frac{1}{2})(\phi 1\frac{1}{2})$.

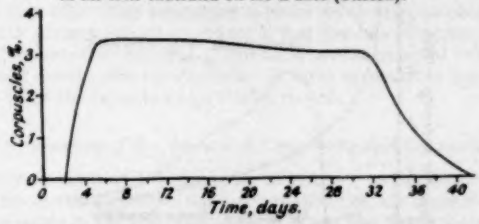
In a similar way the contribution of the active deoxyribonucleic acid formed during the third day to the total deoxyribonucleic acid activity can be calculated and also the share of the deoxyribonucleic acid formed in the course of the first and second day in the total activity

measured on the third day of the experiment can be determined. Each consecutive day we find a new (ϕ) value not represented previously.

As the deoxyribonucleic acid molecules present in the nucleated red corpuscles were found to be entirely stable, not showing any perceptible turnover, the above considerations permit one to determine what percentage, for example, of the labelled red corpuscles formed on the first day is still present in the circulation at any later date. The percentage share of the erthrocytes formed during the first day of the experiment in the total red corpuscle content of the circulation at different dates is shown in Fig. 6.

FIG. 6.

Percentage of hen red corpuscles, formed during the first day of the experiment, present in blood stream at the time indicated on the x*-axis (Ottesen).*

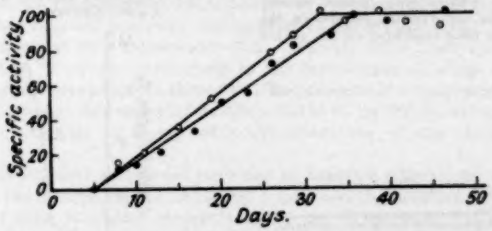


One may be tempted to explain the results obtained by assuming a successive loss of the deoxyribonucleic acid content of red corpuscles during their life-cycle. However, an investigation of the deoxyribonucleic acid content of individual erythrocytes by Ris and Mirsky [47] has shown that this value for each red corpuscle is constant within 10%.

As to a possible objection that not the inorganic but an organic P fraction of the bone marrow is the pertinent precursor of deoxyribonucleic acid, Ottesen has shown that the existence of a deoxyribonucleic acid precursor of considerably lower turnover rate than that of the inorganic P of the marrow is incompatible with the results demonstrated in Fig. 6. A precursor of more rapid turnover rate than that of the marrow inorganic P would clearly not influence the results obtained.

FIG. 7.

Life-cycle of the red corpuscles of two hens. Abscissæ: days after start of experiment; ordinates: specific activity of deoxyribonucleic acid phosphorus extracted from the corpuscles secured at different dates (reproduced, with permission, from Nature, 1945, **156**, 534).



A method very similar to that described above had been used by Shemin and Rittenberg [48] in the determination of the life-cycle of human red corpuscles. They administered glycine containing ^{15}N to human subjects and followed the change with time of the ^{15}N content of hæmin isolated from the erythrocytes. They found this content to decline rapidly after the lapse of 109—127 days. Ottesen based his considerations on the ratio of the ^{32}P content of deoxyribonucleic acid P and its precursor (inorganic P), but Shemin and Rittenberg could not follow such a procedure since the ^{15}N content of the precursor of the hæm nitrogen at different times of the experiment is not known.

Shemin *et al.*[49] applied their ^{15}N technique also to the study of the life-span of the nucleated

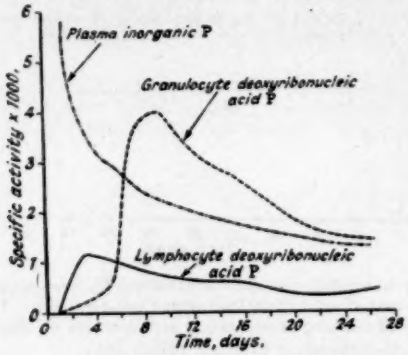
[47] *J. Gen. Physiol.*, 1949, **33**, 125.
[48] *J. Biol. Chem.*, 1946, **166**, 627.
[49] *Cold Spring Harbor Symp. Quant. Biol.*, 1948, **13**, 185.

red blood corpuscles of the chicken. The life-cycle of such corpuscles was found to be about 28 days, in good agreement with the results obtained when using deoxyribonucleic acid ^{32}P as an indicator.

Radio-phosphorus was also applied in life-span determinations in a different way, as described above.[50] By injecting, twice daily, labelled sodium phosphate into the hen, the

FIG. 8.

Change of the specific activity of human-plasma inorganic phosphorus and white-corpuscle nucleic phosphorus with time (Ottesen).



specific activity of the plasma inorganic P was kept at a fairly constant level. As demonstrated by Fig. 7, after the lapse of 33 days the specific activity of deoxyribonucleic acid no longer increased, indicating that only red corpuscles formed during the experiment were now present in the circulation. As significant amounts of labelled red corpuscles were observed only 5 days after the start of these experiment, the life-span of the erythrocytes works out again to be 28 days.

FIG. 9.

Percentage of human lymphocytes, formed during the first day of the experiment, present in the blood stream at the time indicated on the x*-axis (Ottesen).*

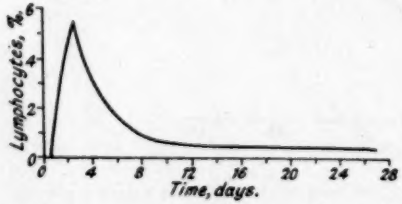
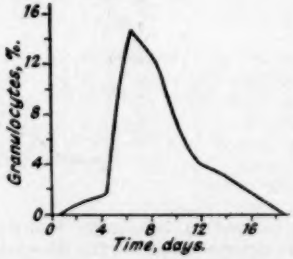


FIG. 10.

Percentage of human granulocytes, formed during the first day of the experiment, present in the blood stream at the time indicated on the x*-axis (Ottesen).*



(b) *Life-time of Human White Corpuscles.*—The same considerations as described above were applied by Ottesen in the determination of the lifetime of human lymphocytes and granulocytes. His results are illustrated by Figs. 8, 9, and 10. In these experiments, not the specific activity of inorganic P of the blood plasma but the corresponding value of the urine inorganic P was determined, as well as the specific activity of deoxyribonucleic acid P of lymphocytes and granulocytes. As with nucleated erythrocytes, the deoxyribonucleic acid molecules present in the white corpuscles were found to remain unchanged during the lifetime of the corpuscles, all turnover being absent. Correspondingly, the ratio of the labelled deoxyribonucleic acid

[50] Hevesy and Ottesen, *Nature*, 1945, **156**, 534.

content of the white corpuscles formed during the first day to that of the totality of circulating white corpuscles is identical with the ratio of the number of white corpuscles formed within the first day to the total number of white corpuscles present in the circulation. It requires a few days before the white corpuscles are formed and released into the circulation. Owing to this, the labelled granulocyte content of the circulation first increases and reaches a maximum after the lapse of 6 days. About 14% of the granulocytes then present are such as were formed during the first day. Their number decreases, however, fairly rapidly with time. After a further 4 days their proportion is reduced from 14 to 7%.

A closer investigation of the number of lymphocytes formed during the first day and still present in the circulation revealed that an appreciable part of lymphocytes present is formed many months before the start of the experiment; thus lymphocytes contain an appreciable proportion of cells of long life. This conclusion is based on the figures obtained for the ratio of the specific activities of plasma (urine) inorganic P and the corresponding value of deoxyribonucleic acid P extracted from lymphocytes. This ratio should be equal to or less than unity for all lymphocytes formed during the experiment. A ratio appreciably higher than unity was, however, found even after the lapse of more than a month.

Determination of the Amount of Circulating Red Corpuscles.

Although the determination of the life-cycle of the red corpuscles necessitates a type of labelling which remains in the corpuscles throughout their life, the measurement of the amount of red corpuscles circulating in the body can be carried out in a few minutes. Hence it suffices to fix the radioactive label to the corpuscles for a comparatively short time. This procedure can be carried out *in vitro*.[51] We secure a blood sample of a human subject, add a few microcuries of labelled sodium phosphate of negligible weight, and shake the material for 1 hour at body temperature. Let us denote the number of red corpuscles injected into the circulation by A, and the ratio of red corpuscles in 1 g. of the injected blood to those in 1 g. of blood secured from the circulation after the injection by B; then the total amount of red corpuscles present in the circulation (x) is given by $x = AB$.

If to 100 ml. of a blood sample kept at body temperature we add labelled sodium phosphate of negligible weight, about one-third of the ^{32}P atoms added are found in the red corpuscles after 1 hour. It follows that in 1 hour—it being assumed that the inorganic P content of the plasma is 4 mg. % and the weight of the plasma constitutes 55% of that of the blood—about 0·7 mg. of inorganic P moves from the plasma into the corpuscles, and *vice versa*. In the course of this interchange some of the ^{32}P added to the plasma penetrates into the red corpuscles and is replaced by ^{31}P atoms moving in the opposite direction.

The red corpuscles contain appreciable amounts of labile organic phosphorus compounds. In glycolytic and other enzymic processes taking place in the erythrocytes these compounds are degraded and resynthesized at a remarkable rate. Shortly after their intrusion as inorganic phosphate most of the ^{32}P atoms participate in the resynthesis of labile organic phosphorus compounds and are incorporated with them.[52] The presence of a comparatively large amount of labile organic phosphorus molecules makes it possible to fix ^{32}P in red corpuscles during an interval which amply suffices to carry out a determination of the circulating erythrocyte volume.

If we suspend the labelled corpuscles obtained in inactive plasma, or inject them into an inactive circulation, the interchange of inorganic P between the labelled red corpuscles and the inactive plasma continues, involving respectively 0·7 mg. of inorganic plasma and corpuscle P in 100 ml. of blood per hour. While, however, during the activation process, together with 0·7 mg. of inorganic phosphorus, ^{32}P of negligible weight and having an activity of 1 μc. moves into the corpuscles, after injection of the labelled corpuscles into an inactive circulation the migration of 0·7 mg. of inorganic P from the red corpuscles into the plasma will be followed by that of about 0·1 μc. only (cf. Figs. 11 and 12). This is because most of the ^{32}P (and ^{31}P) after having penetrated into the red corpuscles finds a temporary abode in the organic phosphorus compounds present in the erythrocytes. About 1/10 represents the ratio of the inorganic P content of the plasma and labile P content of the red corpuscles. This ratio, and correspondingly the time during which ^{32}P is kept in the erythrocytes, may vary for the blood of different subjects. The permeability of the red corpuscle membrane, which is also of importance for the temporary

[51] Hevesy and Zerahn, *Acta Physiol. Scand.*, 1942, **4**, 376; Bohr, *Kgl. Danske Vidensk. Selskab, Biol. Medd.*, 1950, **18**, Nr. 1.

[52] Aten and Hevesy, *Nature*, 1938, **142**, 871.

conservation of ^{32}P in the corpuscles, may vary as well. The loss of the ^{32}P content of the corpuscles in the course of 20 minutes is, however, in no case larger than 3%, and in most cases even appreciably less. When not labelled corpuscles but labelled blood is injected into the circulation, loss of ^{32}P by the corpuscles during the experiment can furthermore be compensated to an appreciable extent by uptake of ^{32}P from labelled plasma present in the circulation.

FIG. 11.

Distribution of inorganic phosphate intruded into the red corpuscles between organic and inorganic fractions.

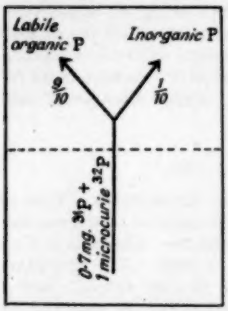
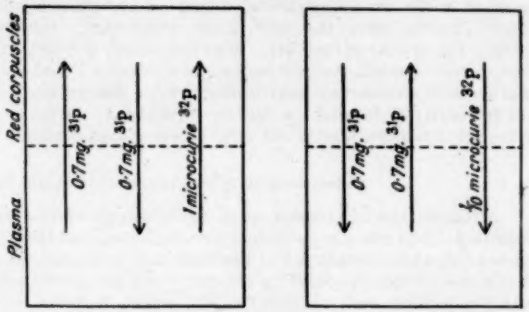


FIG. 12.

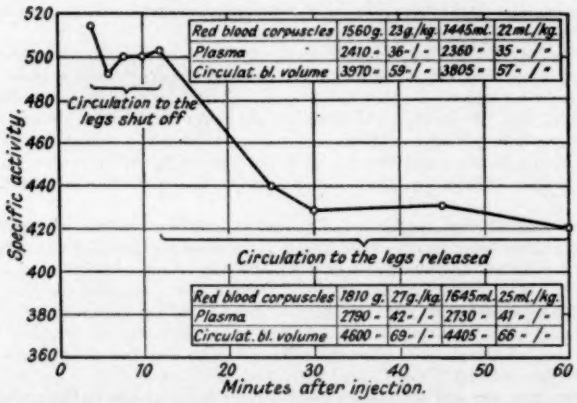
Interchange of ^{31}P and ^{32}P between plasma and red corpuscles.



Nylin [53] made a very extended application of the method described. He determined, besides the total circulating erythrocyte volume, that of single organs such as lungs and legs. A blood sample of a human subject was secured and labelled with ^{32}P as described above. Before injection of an aliquot of the labelled red corpuscles into the subject, the vessels were clamped. The red corpuscles circulating in the legs were thus prevented from participating in

FIG. 13.

Determination of the circulating corpuscle (blood) volume of the legs (Nylin) (reproduced, with permission, from Arkiv Kemi, 1945, **20**, *A*, No. 17).



the " dilution " of the injected labelled erythrocytes, which takes place after injection of labelled red corpuscles into the non-radioactive circulation and the extent of which indicates the amount of circulating erythrocytes. As seen in Fig. 13, 10 minutes after injection of labelled corpuscles, the amount of circulating erythrocytes, excluding that of the legs, is found from the " dilution " figures to be 1560 g. After removal of the clamps, there was a marked decrease in the activity of a 1-g. sample of corpuscle (denoted in Fig. 13 as specific activity). Owing to the participation

[53] *Arkiv Kemi*, 1945, **20**, *A*, Nr. 17, cf. Reeve and Vrall, *J. Physiol.*, 1949, **108**, 12.

of the red corpuscles of the leg in the " dilution " process, the specific activity of the corpuscles decreases from 550 to 428, indicating that the red corpuscle volume of the body, which now includes that of the legs as well, amounts to 1810 g. From the above figures the weight of the erythrocytes circulating in the legs is determined to be 250 g.

The labelling of a red corpuscle sample *in vitro* is made possible by the presence in the red corpuscles of an enzymic mechanism which is instrumental in alternately degrading and building up the comparatively large amounts of labile organic phosphorus compounds in the erythrocytes, and also by the low inorganic phosphate content of the corpuscles, and finally by the fairly slow rate of penetration of phosphate from the plasma into the corpuscles, and *vice versa*.

Red corpuscles can also be labelled by introducing radio-iron, ^{55}Fe or ^{59}Fe. Iron-labelled red corpuscles keep their label throughout their life. As, however, the labelling of erythrocytes with radio-iron can only be carried out *in vivo* it necessitates having blood donors to whom iron of appreciable radioactivity must be administered. Iron-labelled red corpuscles are not applied in the determination of the erythrocyte content of the human circulation. Such corpuscles proved to be useful, *inter al.*, in the study of the post-transfusion survival of erythrocytes preserved during several weeks.

Application of ^{14}C in the Study of Metabolic Depressors and Accelerators.

Although the rapid change in the sensitivity of the indicator during the experiment may be disturbing, as in the study of the mineral constituents of the skeleton (see p. 1630), it is most advantageous when we are interested in restricting the formation of labelled components to a

FIG. 14.

Effect of dinitrocyclopentylphenol on the incorporation of ^{14}C into total fats and total tissue of mice liver. Groups of animals killed at different times after injection of $CH_3 \cdot {}^{14}CO_2Na$ (reproduced, with permission, from Arch. internat. Pharm. Therap., 1951, **86**, 33).

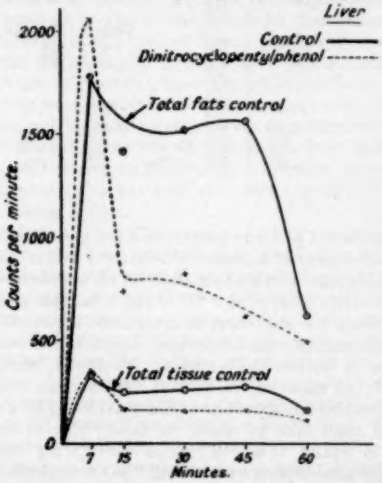
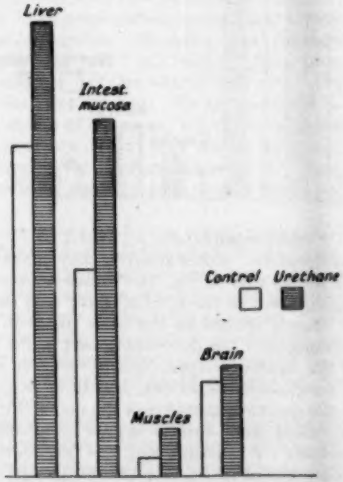


FIG. 15.

Effect of urethane (20 mg.) on the incorporation of ^{14}C into tissue phosphatides. Mice killed 100 mins. after injection of $CH_3 \cdot {}^{14}CO_2Na$.



short time interval. This is the case, as we saw, in the study of the life-cycle of blood corpuscles. The rapid decrease with time in the specific activity of the precursor proves also to be useful in the study of the change of the metabolic rate produced by metabolic depressors or accelerators.

Numerous carbon compounds present in the organism are metabolized at a spectacular rate. Though, as shown by Bloch and Rittenberg,[84] a 100-g. rat by catabolizing fatty acids produces 1 g. of acetate and other tissue constituents per day, the body acetate level of the organism remains very low, owing to the rapid utilization of the acetate produced. This compound is a

[84] *J. Biol. Chem.*, 1945, **159**, 45.

precursor of acetoacetic acid, cholesterol, fatty acids, glycogen, the dicarboxylic amino-acids, proto-porphyrin, uric acid, and the acetyl group formed in many acetylation reactions, with some of which the ^{14}C atoms of acetate are incorporated at a remarkable rate. If we inject labelled acetate into the mouse, the injected radioactive acetate is diluted by non-radioactive endogenous acetate. This dilution rapidly increases owing to the fact that, while the radioactive acetate injected only at the start of the experiment is rapidly metabolized, the endogenous non-radioactive acetate, though rapidly metabolized as well, is newly formed throughout the experiment. The decrease in the specific activity of the body acetate is necessarily reflected in the specific activity of those products with which acetate carbon is incorporated. As resorption, distribution, and conversion of acetate take some time, the ^{14}C content of a rapidly metabolizing fatty acid fraction found to be present in the liver of the mouse after intraperitoneal injection of labelled acetate increases during the first minutes; soon, however, a very rapid decline in the activity figure of the fatty acids is observed.[55] The strongly active fatty acid molecules formed in the initial phase of the experiment are soon metabolized and replaced by molecules formed from less active precursors; correspondingly, a rapid decrease in the fatty acid activity takes place.

FIG. 16.

Effect of urethane on the incorporation of ^{14}C into total fat. Mice killed 110 mins. after injection of $CH_3 \cdot {}^{14}CO_2Na$.

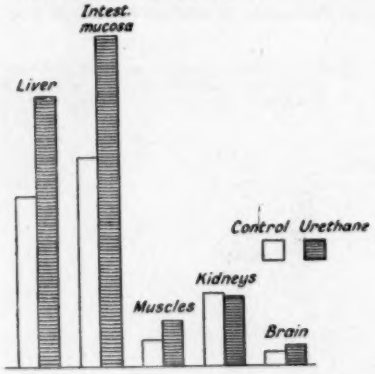
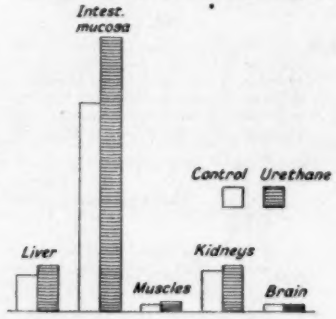


FIG. 17.

Effect of urethane on the incorporation of ^{14}C into tissue proteins. Mice killed 110 mins. after injection of $CH_3 \cdot {}^{14}CO_2Na$.



Dinitro-compounds, *e.g.*, dinitro*cyclo*pentylphenol, when given in proper doses, are metabolic accelerators. Consequently, they enhance the incorporation of acetate ^{14}C into liver fats of the mouse, as seen in Fig. 14.[56] Soon, however, the accelerated metabolism leads to an accelerated replacement of the labelled fatty acid molecules (in which most of the ^{14}C of the total fats is to be found) formed in the early phase of the experiment by molecules formed from less active precursors. The descending part of the curve correspondingly takes a steeper course in the case of the dinitro*cyclo*pentylphenyl-treated animals than in that of the controls. Urethane, which is a metabolic depressor, acts in an opposite way.[57] In experiments taking 100 minutes, thus in the descending region of the curve (Fig. 14), the phosphatide fractions or the total fat (Fig. 16) extracted from various organs of urethane-injected mice take up more ^{14}C than those of the controls. A similar, but less pronounced effect is found (Fig. 17) when comparing the incorporation of ^{14}C into the proteins of organs of urethane-injected mice with the incorporation into corresponding fractions of controls.

In a similar way, acetate labelled in the carboxyl group with ^{14}C was applied in the study of the biochemical effects of ionizing radiation.[58] These investigations revealed an interference, not only, as mentioned previously with the rate of incorporation of ^{14}C into purines of nucleic

[55] Hevesy, Ruyssen, and Beeckmans, *Experientia*, 1951, in print; Beeckmans and de Elliott, *Nature*, 1951, **167**, 200.
[56] Beeckman, Casier, and Hevesy, *Arch. Int. Pharmacodyn.*, 1951, **86**, 33.
[57] Hevesy, *Nature*, 1949, **164**, 1007; Hevesy, Ruyssen, and Beeckmans, *Experientia*, 1951, in print.
[58] Hevesy, *Nature*, 1949, **163**, 869.

acids, but also of other tissue constituents. In the *non-fasting* mouse, for example, irradiation produced a similar effect on the incorporation of ^{14}C into fats and proteins of the brain to that of administration of urethane.

While the disentanglement of the numerous, often competing, metabolic steps involving ^{14}C incorporation and the determination of the extent to which this incorporation is influenced by metabolic depressors and accelerators is a very difficult task, the method outlined above may prove to be a promising approach to the study of metabolic interferences.

The application of radioactive indicators in biochemistry covers a large field and I had to restrict myself to the discussion of a few examples only.

Possible interference of ionizing radiation with the normal biochemical pattern is often considered a disadvantage of the method of radioactive indicators. Such an interference can, however, be avoided by using radioactive tracers of restricted activity. A much more dangerous source of error in the application of radioactive indicators is the non-identity of the chemical properties of isotopes. Tritium, for example, having an atomic mass three times as high as hydrogen, differs from hydrogen to a non-negligible extent in many of its chemical properties. We are witnessing the establishment of a new branch of chemistry which in the course of time may become a very important implement for classical chemistry, namely, that of the rare isotopic constituents. In the long run the claim for accuracy in the biochemical application of isotopic inidcators is bound to increase and it may become necessary to make use of the advances in this new branch of chemistry.

The application of isotopic indicators in biochemistry opened new lines of approach, not only to the solution of known problems, but also by directing our attention to trains of thoughts not considered previously. Some of these ideas I have tried to outline in this lecture. It also induced the experimental chemist to take an interest in the history of the atoms and molecules with which he is dealing.

The chemist is not a historian, he is not interested in the problem whether the carbon atoms of the benzene he is experimenting with were formerly stored in Welsh coal deposits, in carbon dioxide of a volcanic outburst, in the carbonate of crustacea shells, or in a mammalian skeleton. In contrast to the classical chemist, the indicator chemist is to some extent a historian, highly interested in the past of atoms, molecules, and molecular aggregates. He has a great concern in the distinction of how far molecules present in the tissue are " old " or " new." He wishes to know when the potassium atoms present in the tissue cells left the circulation, when the nucleic acid molecules present in the nuclei of thymus cells were formed. He is interested in questions like the former abode or abodes of the carbon atoms of glycogen, the origin of fæces constituents, whether they originate from undigested food or are due to endogenous secretion. He may desire to know which calcium, phosphorus, nitrogen, or sulphur atoms of the plant originate from the soil and which from the added fertilizer, possibly even which from the fertilizing pollen.

Many of the problems attacked by the tracer chemist are such as had been solved previously. The application of isotopic indicators often led to a remarkable simplification of earlier methods. This is the case when measuring circulation rates, water contents, blood volumes, etc. On the other hand, the application of isotopic indicators opened the only way to determine the rate, place, and sequence of formation of many molecular constituents of the living organism. The very existence of such methods was instrumental in opening new trains of thought, in demonstrating the dynamicity of metabolic processes, in confirming Hopkins's statement that " life is a dynamic equilibrium in a polyphasic system," in concentrating our interest on the problem of the velocity of the fundamental biological processes.

Lord Rutherford, who—as Niels Bohr, the preceding Faraday lecturer, so appropriately stated—contributed more than anyone else to the most remarkable development which followed Becquerel's discovery, remarked, when delivering his Faraday Lecture in 1936 : " We can now look back with some sense of perspective and recognize the extraordinary importance of the discovery of radioactivity and the profound influence on a knowledge of atoms and the relation of the elements which has followed from a detailed study of the radioactive bodies." It was this detailed study and the following most remarkable development which made possible the application of radioactive substances as indicators.

PRESIDENTIAL ADDRESS.

DELIVERED BEFORE THE CHEMICAL SOCIETY IN LONDON ON MARCH 20TH, 1951.

Concepts in Catalysis.
The Contributions of Paul Sabatier and of Max Bodenstein.

By E. K. RIDEAL, M.B.E., M.A., D.Sc., F.R.S.

THE ever increasing tempo of research in the natural sciences has rendered it difficult, if not impossible, to follow, far more so to digest, the contributions which are daily being made to each sector of the scientific front. It is thus important for us from time to time to survey the past, and to consider what has proved significant and to note and reject the ephemeral. In judging the importance of any experiment or theory, we must remember that ours is a growing subject. Foundations are intended to be built upon and should not need change, even if the edifice which is arising on them assumes unexpected and indeed in some aspects alarming shapes.

It is the custom in our Society to commemorate the life work of our distinguished Foreign Fellows. Owing to the exigencies of war and the pressure of subsequent events, the homage I would like to offer to two of our most distinguished European Fellows, Paul Sabatier and Max Bodenstein, is somewhat belated but none the less sincere, and it is on their contributions to our concepts in catalysis that I would like to lay special emphasis.

Those that believe in the termite world, to use the words of our former Prime Minister, or consider that distinct types of men are most useful for certain purposes as H. G. Wells's fanciful picture of the inhabitants of the moon suggests, would find it difficult to obtain evidence of any such physical or psychical similarity between these two great men; indeed this is but another example of the fact that the Divine Spirit giving us insight into the ways of Nature, like the wind, bloweth whithersoever it listeth.

Paul Sabatier was born at Carcassonne on November 5th, 1854. In 1874 he went to the École Normale Supérieure from which he graduated in 1877. In 1878 he became assistant to Berthelot at the Collège de France. For his doctorate in 1880 he submitted a thesis on the thermochemistry of sulphur and metallic sulphates. In January 1882 he entered the University of Toulouse, to which he grew greatly attached and where he spent the rest of a remarkably active life. He was released from his posts of Dean and Professor in 1930 but continued to lecture until his death on the 14th of August 1941. He married Mlle. Herail and had four daughters. He was the recipient of many honours, sharing the Nobel Prize with his countryman Grignard; he received the Davy Medal in 1915 and the Royal Medal in 1918. He was a modest and retiring man, loving his work and beloved by his students and co-workers.

Max Bodenstein was born at Magdeburg on July 15th, 1871. In 1889 he went to the University of Heidelberg, where he "promoviert" with Victor Meyer in 1893. After working a short time with Liebermann on organic chemistry and with Nernst on physical chemistry, and completing his military service, he took his degree in Heidelberg in 1899. He then went to Leipzig where he stayed until 1906. Subsequently he was two years at Nernst's Institut in Berlin. From 1908 to 1923 he occupied the chair at the Technische Hochschule in Hanover, succeeding Nernst in Berlin in 1923. In 1936 he was made Emeritus Professor but continued to work in Berlin until his death on the 3rd of September 1942.

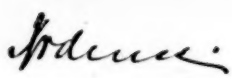
Bodenstein was a great experimentalist and, like Sir William Ramsay, uncannily skilled in the art of glass-blowing. Like many chemists he was a very keen Alpine climber, and during his lifetime gave ample proof of his capabilities as an organiser.

The method of approach to the problems of heterogeneous catalysis by these two investigators was quite different. In 1896 Moissan and Moureu had shown that acetylene reacted with reduced metals, raising them to incandescence. Sabatier decided to use the "less violent" hydrocarbon

Paul Sabatier

[*Reproduced, with permission, from "Les Prix Nobel," 1912.*]

[*To face p. 1640.*



[*Reproduced, with permission, from* Z. physikal. Chem., 1931, Bodenstein-Festband.]

ethylene. On passage of this gas over reduced nickel, at 300° c. a reaction commenced, to give black carbon, and, on analysing the gas formed simultaneously, he was interested to find that it was not hydrogen as he expected but mainly ethane. Clearly the ethylene had undergone decomposition on the surface, the reaction involving a hydrogen transfer. It is interesting to note that this important observation had been ignored until attention was drawn to it quite recently by Beeck, whose untimely death we all deplore. This investigation led Sabatier to examine the catalytic reduction, by hydrogen, of ethylene to ethane and of acetylene to ethylene and ethane. He extended the scope of his enquiry to the various metals when prepared in an active form capable of bringing about hydrogenation and found cobalt, iron, and copper as well as platinum effective, but all less energetic than nickel. He likewise brought about the reduction, till then unaccomplished, of benzene to *cyclo*hexane. In addition to the metals, he showed that certain oxides, *e.g.*, those of zinc and manganese, could bring about the hydrogenation–dehydrogenation reaction, whilst other oxides, *e.g.*, thoria, silica, and alumina, possessed the power of bringing about reversible dehydration–hydration reactions.

When Sabatier commenced his investigation on catalysts little was known about their mode of action, although the phenomenon of catalysis had been well established. The only consistent theory at that time had been propounded by Faraday, who wrote concerning the catalytic combination of hydrogen and oxygen on the surface of platinum : " The course of events when platinum acts upon and combines oxygen and hydrogen may be stated according to these principles as follows. From the influences of the circumstances mentioned, *i.e.*, the deficiency of elastic power and the attraction of the metal for the gases, the latter, when they are in association with the former, are so condensed as to be brought within the action of their mutual affinities at the existing temperature, the deficiency of their elastic power not only subjecting them more closely to the attractive influence of the metal, but also bringing them into more favourable states for union by abstracting a part of that power (upon which depends their elasticity) which elsewhere in the mass of gas is opposing their combination. The consequence of their combination is the production of the vapour of water and an elevation of temperature. But as the attraction of the platina for the water formed is not greater than for the gases, if so great (for the metal is scarcely hygrometric), the vapour is quickly diffused through the remaining gases. The platina is not considered as causing combination of any particles with itself but only associating them closely around it and the compressed gases are as free to move from the platina being replaced by other particles as a portion of dense air upon the surface of the globe or at the bottom of a deep mine is free to move by the slightest impulse into the upper and rarer parts of the atmosphere." Sabatier could not accept this purely physical view of the function of the catalyst, observing that charcoal should on this view be almost a universal catalyst whereas it proved to be somewhat mediocre except for the formation of carbonyl chloride. Again, whilst metals when finely divided absorb considerable quantities of gas, these absorptions are somewhat specific being " characterised by a sort of selective affinity." He noted that some of these reactions are remarkably specific; thus zinc oxide decomposed formic acid into hydrogen and carbon dioxide, but at the same temperature titania gave carbon monoxide and water. We see here the first suggestion that there are two kinds of adsorption, a physical one due to the action of dispersive forces and a chemical one in which an electronic switch is involved.

Sabatier thus formulated a chemical theory of catalysis in which the formation of unstable chemical compounds as intermediary stages is postulated. These determine on his view the direction and speed of the reaction. He stressed the importance of what he termed reciprocal catalysis. Thus hydrogen peroxide solutions decompose relatively slowly in the cold, and the same is true for solutions of chromic acid, but when the two solutions are mixed there is a rapid decomposition with a brisk evolution of oxygen. The decomposition takes place in a proportionate manner corresponding to $3H_2O_2 : 2H_3CrO_6$. The clue to this reciprocal action is to be found in the formation of the dark blue perchromic acid.

Sabatier showed that in several cases definite intermediate compounds could be isolated. Thus in the catalystic oxidation of organic compounds with the aid of copper, or the decomposition of carbon monoxide on nickel, the intermediaries, copper oxide and nickel carbonyl, respectively, can be isolated and identified. For the hydrogenation of ethylene, Sabatier advances arguments for the " fixation," or in modern nomenclature the " chemisorption," of hydrogen by the nickel as the intermediary complex. In the case of acetylene, however, he remarked that it was adsorbed more energetically than hydrogen, thus indicating the possibility of organometallic compounds playing a rôle in heterogeneous catalysis.

On the hypothesis of the existence of intermediary compounds, it is a matter of some interest

to decide whether, for those oxides which bring about the reactions both of dehydration and of dehydrogenation, the same intermediary compound is formed which can decompose in different manners, or whether two different intermediary compounds are formed each with its own particular mode of decomposition. If two different compounds are formed they should possess different properties and the ratios of the quantities of each compound might well be a function of the mode of formation of the surface. We might postulate the existence of an alkyl aluminate undergoing dehydration and a molybdenyl alkoxide undergoing dehydrogenation. This was Sabatier's view and later evidence supports it.

Sabatier summarises his views in respect to the mechanism of catalytic action as follows:

"As far as I am concerned, this idea of temporary unstable intermediate compounds has been the beacon light that has guided all my work on catalysis; its light may perhaps be dimmed by the glare of lights as yet unsuspected which will arise in the better explored fields of chemical knowledge. Actually, such as it is, in spite of its imperfections and gaps the theory appears to us good because it is fertile and permits us in a useful way to foresee reactions."

We must note that Sabatier was the first to demonstrate—and catalytic methods made it possible—the reversibility of the reaction, alcohol $\rightleftarrows$ aldehyde + hydrogen, the progenitor of the now copious thermodynamic and statistical investigations on the free energies of organic reactions. Not only did he demonstrate the selectivity of catalytic action, but also a selectiveness in their sensitivity to poisons; thus the various stages in the catalytic reduction of nitrobenzene by means of hydrogen to *cyclo*hexylamine could be controlled by suitable selective poisons. He noted also the greatly increased activity obtained by spreading a catalyst on a support and, as early as 1897, measured the temperature coefficient of such reactions.

Sabatier termed the chemisorption of reactants on metals "fixation." The metal substrate can be regarded as an electron sink (the vacant *d* bands) or an electron donor (the *s* bands) depending on the nature of the reacting system; *e.g.*, we find for W_2H and Pt_2H that the dipoles are $\overset{+}{W}_2\overset{-}{H}$ and $\overset{-}{Pt}_2\overset{+}{H}$ respectively. As we fill up the surface there are an increasing mutual repulsive interaction between the surface dipoles and a progressive weakening of the interaction between substrate and chemisorbed species. The term "chemisorption" implies a constant and invariant heat of formation, but in those cases which have been examined there is a progressive fall in the heat of sorption. This fall has been attributed to heterogeneity of the surface but the actual form of the curve can be fully accounted for on the basis of an interaction energy. Similar progressive changes are to be noted in the photo-electric and thermionic work functions, and in the ratio of evaporation of atoms to ions in evaporative processes. We may observe that the peculiar effectiveness of nickel as a catalyst may be due in part to the fact that it has not only a $3d^94s^2$ ground state but two excited states $3d^94s^1$ and $3d^{10}$ respectively. It can thus act with ease both as an electron donor and as electron acceptor.

In the case of non-metallic catalysts, *e.g.*, the oxides, the concept of an electron switch is equivalent to an alteration in valency of some constituent catalyst; thus in the catalytic decomposition of hydrogen peroxide on a manganese oxide catalyst we can regard the catalytic operation as essentially a transition from Mn^{++} Mn^{+++} to Mn^{+++} Mn^{++}. The reaction might be formulated as:

$$Mn^{++} + H_2O_2 \longrightarrow Mn^{+++} + OH^- + OH \qquad Mn^{+++} + O_2^- \longrightarrow Mn^{++} + O_2$$

$$H_2O_2 + OH \longrightarrow H_2O + HO_2 \qquad Mn^{++} + HO_2 \rightleftarrows Mn^{+++} + HO_2^-$$

$$HO_2 \rightleftarrows H^+ + O_2^- \qquad H_2O_2 + HO_2 \longrightarrow H_2O + O_2 + OH$$

In this connection Selwood's investigations on the effect of various catalytic supports on the valency of the incorporated catalytic oxide ions seem to me to be of significance, as well as the attention being paid to semi-conducting oxides, *e. g.*, V_2O_5, CeO_2, CuO, and ZnO, as oxidation catalysts, and the photo-conductors such as the sulphides of lead, antimony, and cadmium.

In 1884 van't Hoff's classical work "Étude de Dynamique Chimique" had appeared and this had a great influence on Bodenstein. At that time many cases of so-called "false equilibrium" were cited in the literature, *i.e.*, systems apparently reversible in character but terminating in mixtures of different composition when approached from each end. Included in these cases was the interaction of hydrogen and iodine to give hydrogen iodide,

$$H_2 + I_2 \rightleftarrows 2HI$$

Bodenstein first demonstrated that a true equilibrium could be attained in this system from either end, and then commenced that phase of his investigations to which he devoted the rest of his

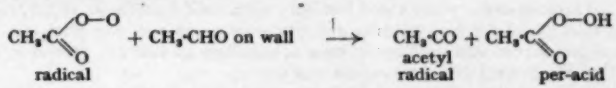
life, namely, the kinetics of gas reactions, commencing with the decomposition of hydrogen iodide and the combination of hydrogen with iodine.

The determination of the absolute rate constants and the influence of temperature permitted Bodenstein to test the applicability of the kinetic theory. As we now know, these particular reactions were eminently suitable for such an examination since the molecules involved were relatively simple. These reactions, together with the decomposition of dinitrogen tetroxide, have proved to be the corner stones of the theory of bimolecular gas reactions.

Bodenstein then investigated termolecular reactions such as $2NO + O_2$ and the reactions of nitric oxide with the halogens. Later he showed that these were really sequent reactions and he could account for a negative temperature coefficient on the assumption of the sequence :

$$(1)\ 2NO \longrightarrow N_2O_2$$
$$(2)\ N_2O_2 + O_2 \longrightarrow 2NO_2$$

The classical work of Bunsen and Roscoe on the hydrogen–chlorine reaction was next examined, and the concept of chain reactions in which atoms served as chain carriers permitted Bodenstein to gain an insight into the reactivities of free atoms and radicals, and the mechanism of operation of inhibitors such as oxygen, ammonia, water vapour, and the walls of the containing vessel. These experiments in turn led to the principle of detailed balancing and the concept of quasi-stationary states in which each sequent reaction could be examined for entropy or steric factors, thermal changes, and activation energies. For the combination of atoms, Bodenstein showed that a three-body collision was necessary. In the autoxidation of acetaldehyde he postulated the formation of intermediary reactive radicals

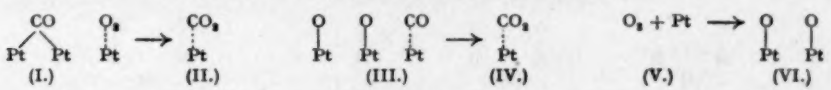


Bodenstein's approach to the problems of heterogeneous catalysis was naturally from the kinetic standpoint : under what conditions do the rate of transport or reactants to the catalyst, the rate of reaction at the catalyst surface, and, finally removal of products from the catalyst govern the overall rate of reactions?

On investigating the combination of sulphur dioxide and oxygen at the surface of platinum, Bodenstein concluded that the rate of combination was governed by the rate of diffusion of the sulphur dioxide to the platinum, through the layer of sulphur trioxide, a view slightly reminiscent of that of Faraday. He applied similar considerations to the catalytic oxidation of carbon monoxide at the surface of crystalline quartz and quartz-glass, the reaction in the latter case being inversely proportional to the pressure of carbon monoxide.

In 1916 Langmuir published his well-known paper on the catalytic oxidation of carbon monoxide and of hydrogen at the surface of platinum. He showed that the formal reaction kinetics of the carbon monoxide oxidation at a platinum surface, even at very low pressures, obeyed the same laws as Bodenstein found for the reaction at a fused-quartz surface. Langmuir showed *inter alia* that carbon monoxide, oxygen, and hydrogen when chemisorbed on platinum occupied two elementary lattice spaces or that the surface compounds were bivalent in respect to carbon monoxide and that both hydrogen and oxygen formed elementary hydrides and oxides.

The oxidation of carbon monoxide did not take place between two neighbouring chemisorbed species and of the various alternative processes which can be depicted as :



reactions (III) ⟶ (IV), and (V) ⟶ (VI), proceed much more readily than (I) ⟶ (II). We may regard the carbon monoxide when adsorbed as relatively inert or as a poison. It can be considered in the light of a co-ordination compound with closed (complete) electron shells, having in consequence a high ionising potential rendering electron transfer a difficult operation. The reaction competing with (I) ⟶ (II) is the evaporation of carbon monoxide.

It is possible that the views of Sabatier in respect to a " fixation " or formation of an intermediary compound, which received such precise formulation by Langmuir's concepts of surface atomic centres' being equivalent to free radicals in reactivity, modified Bodenstein's views. For we find that in his later investigations in respect to heterogeneous catalysis Bodenstein

gave up the diffusive hypothesis. He found, for example, that the decomposition rate of stibine at an antimony surface was governed by the rate of reaction at the surface itself. He also devoted a good deal of attention to the catalytic oxidation of ammonia to oxides of nitrogen and in one of his later papers he considered the mechanism as involving a series of reactions in which the initial one entailed interaction of gaseous ammonia and chemisorbed oxygen. His formulation can be expressed in the form of the following possible reactions:

$$(1)\ NH_3 + Pt_xO \longrightarrow NH_2O \text{ (hydroxylamine)}$$

$$(2)\begin{cases} NH_2O + O_2 \longrightarrow HNO_3 + H_2O \\ 4HNO_3 \longrightarrow 4NO + 2H_2O + O_2 \end{cases}$$

$$(3)\begin{cases} NH_2O + NH_3 \longrightarrow N_2 + H_2O + 2H_2 \\ 2H_2 + O_2 \longrightarrow 2H_2O \end{cases}$$

$$(4)\begin{cases} NH_2O + Pt_xO \longrightarrow HNO + H_2O \\ 2HNO \longrightarrow N_2O + H_2O \end{cases}$$

Bodenstein noted that if hydroxylamine were an intermediary its fate could be decided by separate experiment. He studied first the decomposition of the gas from room temperature to 200° C. and showed that decomposition occurred as a wall reaction:

$$\begin{array}{l} 2NH_2{\cdot}OH \longrightarrow NH(OH)_2 + NH_3 \\ 2NH(OH)_2 \longrightarrow N_2O + 3H_2O \\ \hline 4NH_2{\cdot}OH \longrightarrow N_2O + 2NH_3 + 3H_2O \end{array}$$

Above 200° C. no nitrous oxide was formed but only nitric oxide, nitrogen, water, and ammonia.

To test reaction (3) he passed ammonia and hydroxylamine over hot platinum. At 180° C. some reaction was observed and decomposition was complete at 400° C. However, no hydrogen was found. This eliminated (3) as a possible reaction.

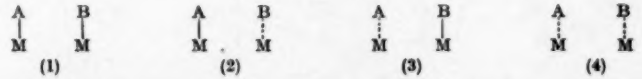
To examine the possibility of reaction (4) he passed hydroxylamine over iron–bismuth oxide, a technical catalyst for the oxidation of ammonia. At 200° C. he obtained some nitric oxide and ammonia with very little hydrogen, the chief product being nitrous oxide, indicating that (4) is a reaction of major importance. We must note, however, that these results of Bodenstein can likewise be interpreted on the hypothesis that a platinum imide and not hydroxylamine is an intermediary in the reaction:

$$\underset{\text{ads.}}{NH_3 + Pt_xO} \longrightarrow H_2O + \underset{\text{ads.}}{Pt_xNH}$$

followed by

$$Pt_xNH + O_2 \longrightarrow HNO_3 \longrightarrow NO + NO_2 + H_2O$$
$$Pt_xNH + NH_3 \longrightarrow N_2H_4 \longrightarrow N_2 + H_2 + NH_3$$

N_2O being formed by a secondary reaction $Pt_xNH + Pt_xO \longrightarrow HNO \longrightarrow N_2O$. We note with interest the conclusions which Bodenstein reached with respect to the actual reaction mechanism, *viz.*, between a chemisorbed species, the oxygen in the form of a surface oxide Pt_xO and a physically adsorbed ammonia. For two reactants A and B undergoing reaction at a metal catalyst surface to form a product C, even if we ignore the complications which may be introduced by the presence of the product, there are evidently several possible processes. If we denote by — a chemisorbed link and by ···· a physically adsorbed species we have the following possible choices:



The reaction complex (4) represents Faraday's mechanism which, as we have seen, must be rejected. The choice between (2) and (3) naturally depends on the nature of A and B respectively.

Bodenstein chose the oxygen to form the surface oxide Pt_xO as the reactant. In oxidative reactions more recent work has supported his views, for oxygen will in many cases displace other chemisorbed species, *e.g.*, hydrogen from tungsten. It is, however, not so evident that oxygen undergoes chemisorption to form the surface oxide, $M_x + O_2 \longrightarrow 2M_xO$, in one elementary act. Thus on tungsten there is evidence for the primary formation of an unstable oxygen complex before conversion at higher temperatures into the more stable W_xO state. That oxygen atoms can be removed by evaporation at high temperatures is not conclusive

evidence for their presence on the surface; thus it is difficult to distinguish the mechanisms where the following thermal changes are involved :

Sabatier noted the variation in catalytic activity between copper, which had been slightly oxidised, and cupric oxide which is formed above 500° c. On slightly oxidised copper the reaction between hydrogen and oxygen takes place by means of the following interesting coupled reactions :

$$Cu_s + O_2 + H_2 \longrightarrow Cu_2O + H_2O$$

which at higher temperatures is followed by a reaction

$$Cu_2O + H_2 \longrightarrow Cu_s + H_2O$$

The energy of activation of the coupled reaction is *ca.* 6500 cals./g.-mol., which is remarkably close to the work function for the elevation of electrons from the sources into the conducting bands of the semi-conducting cuprous oxide (*ca.* 0·35 volt). One might suggest that the detailed mechanism might be represented as

$$\begin{array}{ccc} & O_2 \quad H_2 & \\ Cu & Cu \quad Cu & \\ Cu & Cu^+ \quad Cu & \end{array} \longrightarrow \begin{array}{ccc} & O^- \quad OH_2 & \\ Cu & Cu^+ \quad Cu & \\ Cu & Cu^+ \quad Cu & \end{array}$$

On strongly oxidised copper the combination of the hydrogen proceeds in a perfectly stoicheiometric manner to water with a much higher energy of activation which is comparable to that obtained for the activated diffusion of the hydrogen in copper oxide, and the reaction scheme might be represented as :

$$\begin{array}{cc} O^- & H_2 \\ Cu^+ & Cu \end{array} \longrightarrow \begin{array}{cc} O^- & H_2^+ \\ Cu^+ & Cu^- \end{array} \longrightarrow \begin{array}{ccc} OH_2 & & \\ Cu & Cu & \end{array}$$

A similar reaction scheme could be proposed for the oxidation of carbon monoxide on a slightly oxidised copper surface.

It is perhaps significant in this last reaction that on copper oxide there is no exchange of isotopic oxygen between oxygen and carbon dioxide until temperatures in excess of 500° are attained, suggesting that the reaction $Cu_2O + CO_2 \longrightarrow Cu_2CO_3 \longrightarrow Cu_2O + CO_2$ requires a relatively high energy of activation, whilst the catalytic oxidation of carbon monoxide itself will proceed at 120°.

Bodenstein, as we have observed, chose as the reaction system one involving in the ultimate analysis reaction between a chemisorbed and a physically adsorbed species. Langmuir's analysis of the catalytic oxidation of carbon monoxide led him to similar conclusions. The entropy changes involved may prove to be an important factor in determining the velocity of any particular reaction system. A good example of such has recently been examined by Kemball who has shown that of the two reactions which may be written :

$$\begin{array}{ccc} CH_4 & D & \\ \vdots & | & \\ Ni & Ni & \end{array} \longrightarrow \begin{array}{ccc} CH_3 & H & \\ | & | & \\ Ni & Ni & \end{array} \quad \begin{pmatrix} \Delta H = -6{\cdot}4 \text{ kcals.} \\ \Delta E = 24 \text{ kcals.} \end{pmatrix}$$

and

$$\begin{array}{cccc} CH_4 & D & D & \\ \vdots & | & | & \\ Ni & Ni & Ni & \end{array} \longrightarrow \begin{array}{ccccc} CH_2 & & H & H & \\ & \diagdown & | & | & \\ & & Ni & Ni & \end{array} \quad \begin{pmatrix} \Delta H = -12{\cdot}8 \text{ kcals.} \\ \Delta E = 32 \text{ kcals.} \end{pmatrix}$$

the second reaction proceeds more rapidly than the first (the former loosing some 15 e.u. and the latter gaining some 20 e.u. in the process). The reaction between two chemisorbed neighbours is favoured by the entropy changes, but there are also certain basic assumptions involved : first, that the dipolar repulsive forces shall be small and identifiable with the energy of activation, and, secondly, that one or both of the chemisorbed species shall be mobile at the temperature of catalysis. Thus in the combination of hydrogen and oxygen at a platinum surface it

would appear that under certain conditions the reaction apparently involves the interaction between chemisorbed neighbours and it is possibly significant that the dipoles formed in this case from the reactants are opposite in sign, *i.e.*, Pt_zH^+ Pt_zO^-.

We are now reasonably confident that in many cases, if not all, of physical adsorption there is some measure of surface mobility, at any rate under the conditions of temperature and vapour or gas pressures usually involved. In the case of chemisorption, however, direct evidence is not so clear.

To identify the energy of activation of the catalytic process with the removal of the electron from the source into a migrating level, as we have seen in the case of the reduction of cupric oxide, is an over-simplification, for here we appear to demand the presence only of electron sinks in the substrate, *e.g.*, Cu^{++} or oxygen (in N-type semi-conductors). Again we note that the electron has a considerable range of motion from source to conducting level to sink, and the impurity or electron source or electron sink itself does not necessarily move. It is known, however, that these sources and sinks do begin to move at elevated temperatures (*e.g.*, movement of K^+ and Cl^- in the KCl lattice) and contribute to the conductivity.

The distinction between a mobile and an immobile film may be detected in those cases where repulsive forces exist between the chemisorbed species by the rate at which the surface fills up. If the interaction energy for the chemisorption of hydrogen be of the order $\epsilon/RT = 9{\cdot}0$, this rate is given in the following Table.

θ.	Ratio of time for filling, $\frac{\text{mobile}}{\text{immobile}}$	θ.	Ratio of time for filling, $\frac{\text{mobile}}{\text{immobile}}$
0·1	1·0	0·6	$2{\cdot}8 \times 10^3$
0·3	1·06	0·7	$9{\cdot}7 \times 10^3$
0·4	1·20	0·8	$1{\cdot}9 \times 10^3$
0·5	2·97	0·9	$12{\cdot}0 \times 10^3$

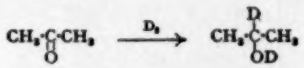
We note that at $\theta = 0{\cdot}5$, when the film is mobile, the surface will, owing to the operation of the repulsive forces, tend to acquire a regular checker board arrangement. Subsequent adsorption will be dependent on fluctuations in this arrangement and thus proceed much more slowly than for an immobile film. It would appear with this criterion that chemisorbed oxygen becomes mobile on metals only at relatively high temperatures. The third factor which must play a part in such a mechanism is the surface atomic spacing. This indeed is important also in cases (2) and (3), where the act of chemisorption involves interaction with more than one atom of the substrate, *e.g.*, in chemisorption of hydrogen or of an unsaturated hydrocarbon. The hydrogenation of ethylene at various metallic surfaces is a good example of this fact, so much insisted upon by Balandin; the range of atomic spacing operative lying between 3·2 and 4·5 A. with an optimum at *ca.* 3·75 A. (rhodium).

It is still a much debated problem whether relatively large portions of a catalytic surface, *e.g.*, specific crystal surfaces containing appropriately spaced atomic centres, are the seat of catalytic activity or whether highly localised active patches, *e.g.*, lattice defects, are responsible. The concept of active patches has been supported on several grounds. The form of the ΔH–θ curve has been advanced in support of the former postulate.

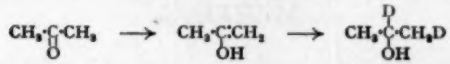
We have seen that such a falling off in ΔH values with surface coverage can be accounted for by considerations already advanced in interpreting electron, ion, and atom emission from monolayer-coated emitters. If an active-patch interpretation is to be advanced it is evident that the lifetime of the adsorbed species either on the surface or in the same spot (surface mobility) must be short compared with the duration of the experiment. This does not appear to be the case for values of $\theta < 0{\cdot}5$ where ΔH attains relatively high values. The selectivity of poisons has likewise been advanced to support the concept of active patches. Here again surface mobility of the poison is a *sine qua non*. Interpretations based upon multi-point contact of a reactant lead to forms of curves which do in fact reproduce those experimentally obtained and which are frequently interpreted on the active-patch view.

If a small quantity of deuterium is admitted to a nickel catalyst and this is followed by the admission of a small quantity of hydrogen, on evacuation of the system the first samples of gas to be removed are rich in hydrogen. If we reverse the procedure, the gas is found to be rich in deuterium. This experiment has been cited in support of the view that the surface of the nickel is energetically heterogeneous. We note, however, that diffusion of the gas into the interior of the nickel would achieve the same results.

Whilst the results of the use of isotopic hydrogen in this particular experiment cannot be interpreted in a unique manner, there are, however, many cases where the use of deuterium or tritium or other radio- or mass isotopes does contribute to our proper understanding of the reaction mechanism. Thus, for example, in the catalytic hydrogenation of acetone at low temperatures the reaction proceeds as follows :



whilst at higher temperatures there is an increased intervention of the reaction,



We have noted that the formation of a chemisorbed species involves an electron transfer and that the subsequent catalytic reaction involves a similar passage of an electron. This again emphasises the necessity for the presence of electron sources and electric sinks in the catalyst itself. These, as we know especially from work on semi-conductors and binary alloys, may be increased or decreased by the inclusion of electron donors or acceptors in the catalyst or its support. In the sense that an electron switch is involved in the catalytic action, these sources or sinks may be regarded as active patches, but it is clear that if the electron can travel, as indeed it can in conductors and semi-conductors, a long distance between source and sink, the active patches need not be near the surface at all.

In this review I have attempted to show that, in the contributions of Paul Sabatier and Max Bodenstein to our knowledge of the mechanism of heterogeneous catalysis, there is much of permanent value but also there is still much to be discovered before Sabatier's beacon light suffers eclipse.

ONE HUNDRED AND TENTH ANNUAL GENERAL MEETING.

THE One Hundred and Tenth Annual General Meeting of the Chemical Society was held in Burlington House, at 11.30 a.m. on Wednesday, 21st March, 1951. The President, Professor E. K. Rideal, was in the Chair.

The Notice convening the Meeting was read.

The Senior Secretary, Professor D. H. Hey, in presenting the Report of Council for 1950 stated that the Fellowship had continued to increase although not so rapidly as in the immediate post-war years. However, numbers rose in 1950 by nearly 2% and this figure would have been larger had not 107 names of Life Fellows and of those formerly in enemy, or enemy-occupied, countries, with whom the Society had lost touch, been removed from the register, their Fellowship being deemed to have lapsed. The "turn-over" of Fellows had continued at a high rate and emphasised the need for an active policy of recruitment of new Fellows.

As was usually the case, the section of the Report that dealt with Publications was perhaps the most important. Most of the arrears of publications were overtaken in 1949 and had it not been for the increased rate of submission of new papers the *Journal* might have declined in size. In the event, however, there was no diminution in the publication rate which is bound to increase still further. By the beginning of the week the Society had received 188 papers since January 1st. Comparable figures for 1950 were 170 and for 1949, 112. It was significant that, despite the larger number of papers received, the proportion from Industry and from Overseas continued to increase. This year would see the publication of an Editorial Report on nomenclature issued with the Index for 1950 to be published in April, 1951. It is the first of what will, it is hoped, become an annual series of value to Fellows wishing to keep in touch with nomenclature developments. In 1950, also, arrangements were made for the issue, in 1951, of two special publications—the Cumulative Index to the Annual Reports and another Volume, Volume IV, of Memorial Lectures.

An event of very great potential importance for the Society was the proposal, announced by the Lord President of the Council, to build a Science Centre in which the Chemical Society would have accommodation worthy of its importance and adequate for its needs. The Society was very much indebted to Sir Robert Robinson who, as President of the Royal Society, had most ably represented the needs of the Scientific Societies in the negotiations with the Government.

In conclusion, Professor Hey paid a tribute to the work of the permanent staff of the Society and expressed the thanks of the Council to those who had served the Society in many ways: by helping with its publications, by service on committees, or as Local Representatives.

The Accounts for 1950 were presented by the Treasurer, Sir Wallace Akers, who described the results as satisfactory, having regard to the very difficult circumstances of a year in which prices had continued to rise and the spending power of individual Fellows was progressively reduced.

The adoption of the Report and of the Accounts was moved by Professor A. R. Todd who praised especially the vigorous publication policy of the Society. Professor Todd's motion was seconded by Professor C. W. Shoppee, and the Report and the Accounts were unanimously adopted.

The President then announced the following new elections to the Council of the Society (including those elected as a result of the Report of the Scrutators on the ballot which had recently been held) :

Vice-Presidents who have not filled the Office of President :

Professor G. H. Clemo.
Professor D. H. Hey.
Professor M. Stacey.

Honorary Secretaries :

Professor E. D. Hughes.
Dr. L. E. Sutton.

Elected Ordinary Members of Council :

Constituency I :	*Constituency II :*	*Constituency III :*
Dr. H. M. Powell.	Professor Wilson Baker.	Dr. G. Baddeley.
Dr. H. N. Rydon.	Professor C. W. Shoppee.	
Dr. J. W. Smith.		
Constituency IV :	*Constituency V :*	*Constituency VI :*
Dr. T. S. Stevens.	Dr. J. Bell.	Professor A. R. Ubbelohde.

The President then referred to the great service rendered to the Society by Professor Hey who was retiring from the Office of Honorary Secretary which he had held for five years.

On the motion of Mr. P. A. Briscoe, seconded by Dr. G. A. Swan, Messrs. W. B. Keen and Co., were re-appointed as the Society's Auditors for 1951.

The business was concluded by a vote of thanks to the Officers and Council for their services in the past year, which was proposed by Professor J. M. Robertson, seconded by Dr. M. A. T. Rogers, and carried with acclamation.

REPORT OF COUNCIL FOR 1950.

I. FELLOWSHIP.

1. *General.* In the year 1950 the number of Fellows increased by 158, and on December 31st there were 8353 names on the Register. Elections totalled 749 and 29 Fellows were reinstated. The Society has lost 66 Fellows by death and 267 by resignation. Fellows removed from the Register numbered 288, including 107 with whom the Society has lost touch and whose Fellowship is deemed to have lapsed.

The number of Fellows participating in the Joint Subscription Scheme sponsored by the Chemical Council was 4750 or 56·9% of the total Fellowship.

Joint Student Facilities were granted by the Chemical Council to 19 persons. The number of Students subscribing under these arrangements now totals 47.

2. *Honours.* The Council has conveyed the congratulations of the Society to the following Fellows whose names have appeared in the New Year and Birthday Honours Lists :

Knight Bachelor

Dr. W. R. Grimwade
Dr. J. I. O. Masson
Dr. J. E. Myers
Dr. S. J. Saint

C.B.

Dr. O. H. Wansbrough-Jones

C.B.E.

Dr. F. Hardy
Dr. H. King
Professor F. G. Soper
Dr. A. J. Turner

Congratulations have also been conveyed to Professor T. Reichstein, *Honorary Fellow*, on the award of a Nobel Prize for Medicine and to Sir John Simonsen on the award of a Davy Medal by the Royal Society.

3. *Deaths.* Among the Fellows whom the Society has lost by death the Council wishes to record with profound regret the death of the two distinguished past Presidents of the Society and of the two former Vice-Presidents and Honorary Secretaries whose names are given below. Obituary notices will be published.

Sir Norman Haworth (*President* 1944—1946).
Professor W. P. Wynne (*President* 1923—1925).
Professor C. S. Gibson (*Vice-President* 1933—1936, 1942—1945; *Honorary Secretary* 1924—1933).
Professor S. Sugden (*Vice-President* 1939—1942, 1946—1949; *Honorary Secretary* 1933—1936).

II. PUBLICATIONS.

1. *Journal.* In the January and February issues of the *Journal* the last arrears of publication were overtaken; and thereafter there were no avoidable delays in publication.

For some time past, the *Journal* had been issued regularly, but a month late, *i.e.*, the issue dated for a month "x" had been available about the end of the month "$x + 1$", instead of at the end of the month "x" as in pre-war years. In the Spring of 1950, this was remedied by publishing four successive issues at about three-weekly intervals. The effect of this has been that twelve issues were published in eleven months of 1950. Thus,

while figures recorded below for Communications received refer to the whole of 1950, those for Communications published refer to only eleven months.

During 1950, 874 Scientific Communications were received, 27 were declined, and 41 withdrawn. The *Journal* contained 824 items, made up as follows:

Papers (General, Physical, and Inorganic)	147
,, (Physical Organic)	110
,, (Organic)	470
Notes	73
Lectures and Addresses	6
Obituary Notices	16
Annual General Meeting	1
Editorial Nomenclature Report	1

Scientific Communications from overseas, published during 1950, numbered 136 (a few jointly with British laboratories), as follows: Australia 51, Czechoslovakia 1, Denmark 1, Egypt 13, France 3, Hungary 1, India 1, Irish Republic 8, Israel 6, New Zealand 22, S. Africa 14, Spain 1, Switzerland 1, U.S.A. 12, Yugoslavia 1.

Contributions from industrial laboratories totalled 111 (including 22 jointly with academic institutions), and those from industrial research organisations and Government laboratories totalled 40 (including 9 jointly with academic institutions). The increase in the proportion of communications from industrial laboratories (from 11·6% to 13·7%) may be significant.

The high rate of publication reached in 1949 was maintained in 1950, but, whereas in 1949 this enabled arrears to be published, in 1950 it was required to deal with the larger number of papers received:

	1948.	1949.	1950.
Papers and Notes received (less number rejected or withdrawn)	531	720	806
Papers and Notes published	511	870	806 *
No. of pages (Papers and Notes)	2203	3762	3576 *
No. of pages (total, excl. indexes)	2330	3858	3697 *

* Twelve issues published in eleven months.

The number of papers and notes (806) published during eleven months of 1950 is equivalent to 879 during a full year; the excess over the number for publication (fortuitously also 806) constitutes the arrears published in the January and February issues plus the general acceleration of publication. The average number of pages per paper rose slightly, from 4·35 in 1948 and 4·32 in 1949 to 4·44 in 1950.

The normal time between the receipt of a manuscript and its publication was 4½ months. For instance, of 171 papers published in the November and December issues, 110 (64%) were published within five months of receipt; of these, 28 were published within four months of receipt. The delay to most of the remainder was caused by authors' consideration of the referees' comments.

A slight improvement in format was possible during the year: a line space introduced between paragraphs of the smaller size of type considerably improved legibility.

2. *Nomenclature.* An Editorial Report on Nomenclature is being published with the Index to the *Journal* for 1950. It is hoped to issue, each year, similar reports on developments in nomenclature as practised in the Society's publications. Reprints of the Report for 1950 are available, price one shilling, post free.

3. *Microfilm Edition of the Journal.* The Society has entered into an agreement to make issues of the *Journal* from January 1950 available in microfilm form. It is hoped that this will be of assistance to libraries faced with problems of storage Sales are restricted to subscribers to the paper edition, and the film copy is distributed only at the end of the year.

Enquiries regarding purchase should be made to University Microfilms, 313 N. First Street, Ann Arbor, Michigan U.S.A.

4. *Early Volumes of the Journal.* Volumes 1 to 23 of the *Journal* (1848–1870) have been reprinted, under an agreement with the Society, by Messrs. Butterworths (Scientific Publications), Ltd. In addition, a survey of holdings in libraries and elsewhere has been made. The information which has been obtained will determine whether any further arrangements are necessary for the re-issue of early volumes of the Society's Publications.

5. *Annual Reports on the Progress of Chemistry.* In accordance with the ruling of the Publication Committee made after the *Quarterly Reviews* became established, the *Annual Reports* are reverting to a series of annual, or for some subjects bi - or tri-ennial, records of progress. The Reports for 1948, 1949, and 1950, are, however, in some sections, transitional in character and contain review articles.

The Council has authorised an increase of up to 50% in the size of the *Annual Reports* for 1950.

6. *Cumulative Index to the Annual Reports.* Fellows placing an order before January 31st, 1951, have been given the opportunity to buy a copy of the Cumulative Index to the *Annual Reports*, Vol. I (1904)–Vol. XLVI (1949), at the special price of twelve shillings and sixpence. This index will be published in June 1951 at a price of twenty-five shillings. The entries in this index which refer to Volumes I—XLII (1904—1945) were collated by British Chemicals and Biologicals, Ltd., to whom the Council of the Society expresses its grateful appreciation and thanks.

7. *Quarterly Reviews.* Volume IV (1950) of *Quarterly Reviews* contained nineteen articles, occupying 425 pages. (Vol. III, 1949, nineteen articles, occupying 384 pages.)

8. *Memorial Lectures, Volume IV.* The Council has authorised the publication of a further volume of collected Memorial Lectures reprinted from the *Journal*. It is hoped that this will be issued during 1951. Full particulars will be announced in the *Proceedings*.

III. MEETINGS.

1. *Scientific Meetings.* Eleven Meetings were held in London during 1950. These included four Lectures and one Symposium. At the other six Meetings, fifteen Papers, or series of Papers, were read and discussed.

84 meetings arranged by Local Representatives on behalf of the Society, or held in conjunction with other bodies, took place outside London. In addition, Fellows were able to attend, under arrangements made locally, a number of meetings organised by other Societies.

Official Scientific Meetings of the Society were held as follows :

Birmingham	February 10th
Manchester	October 19th
Southampton	November 17th
Bangor	November 23rd

Details of all Meetings are given in Appendix A.

2. *Anniversary Meetings.* The Anniversary Meetings were held in Edinburgh on March 29th and 30th. The Presidential Address, " The Chemical Society—A Mid-Century Review ", by Sir Ian Heilbron (*J.*, 1950, 1641) was given and the One Hundred and Ninth Annual General Meeting, which was reported in the *Journal* for June 1950, was held on the morning of Wednesday, March 30th. Coach Tours were arranged on the same afternoon to the Forth Bridge and to the Border Country, and at 8.30 p.m. a Reception given by the University of Edinburgh was held in the University Library.

On Thursday, March 30th, after the Annual Meeting of Local Representatives, the Faraday Lecture, " The Application of Radioactive Indicators in Biochemical Studies ", was delivered by Professor G. Hevesy, For.Mem.R.S., *Honorary Fellow*. At the Anniversary Dinner, held that same evening, Professor E. K. Rideal was formally installed as President of the Society.

3. *Centenary Lectures.* In March, Professor Dr. Pl. A. Plattner (Zurich) was invited to visit this Country to lecture. In addition to a Meeting in London on March 2nd, Professor Plattner also lectured in Dublin, Liverpool, and Manchester.

The Society also invited Professor H. Erdtman and Mrs. G. Aulin-Erdtman (Stockholm) to take part in the Symposium on " Tropolones and Allied Compounds ".

IV. LIBRARY.

The Annual Report of the Joint Library Committee for 1950 is reproduced as Appendix B to this Report.

V. OTHER ACTIVITIES.

1. *Accommodation.* Difficulties caused by the acute shortage of accommodation have been referred to in previous Reports. A solution of this problem was brought a stage nearer when the Lord President of the Council announced that His Majesty's Government had agreed to build a Centre to house a number of Scientific Societies including those at present accommodated in Burlington House.

This announcement, however, gives no solution of the immediate difficulties of the Society, since it is certain that the proposed new buildings will not be completed for a considerable number of years.

2. *Grants for Research.* The Council has authorised grants totalling £877 15*s.* 0*d.* to be made from the Research Fund to 29 applicants.

3. *Harrison Memorial Prize.* The Harrison Memorial Prize for 1950 has been awarded to Dr. H. C. Longuet-Higgins.

4. *The Chemical Council, and the Bureau of Abstracts—Reports for* 1949. Fellows may obtain copies of these Reports from the General Secretary.

VI ADMINISTRATION.

1. *Council.* At the Annual General Meeting on March 29th, the following were declared elected :

President	Professor E. K. Rideal
Vice-President	Professor R. P. Linstead
Elected Ordinary Members of Council...	Dr. J. S. Anderson, Professor F. E. King, Dr. L. N. Owen, Professor L. Hunter

Since the Annual General Meeting the following changes have taken place in the Membership of Council :

Honorary Secretary : Professor E. D. Hughes was appointed under Bye-Law 42 in place of Dr. Alexander King who resigned.

Ordinary Members of Council : Dr. G. Baddeley was appointed under Bye-Law 42 to fill the vacancy caused by the death of the late Dr. A. E. Gillam. Professor Gwyn Williams was appointed under Bye-Law 42 in place of Professor F. S. Dainton, who resigned under Bye-Law 56.

2. *Local Representatives.* The Council received with regret the resignation of a number of Local Representatives, and the following new appointments were made :

Leeds	Mr. P. A. Briscoe in place of Dr. F. R. Goss
Manchester	Dr. G. R. Barker in place of Dr. G. Baddeley
Newcastle	Dr. G. A. Swan in place of Dr. P. L. Robinson
St. Andrews and Dundee	Dr. H. T. Openshaw in place of Dr. J. D. M. Ross

Dr. L. E. Sutton served as Local Representative for Oxford during the absence, in the United States, of Dr. W. A. Waters.

In order to improve the service to Fellows who are not able to attend meetings in London, arrangements have been introduced whereby the Society's Office in London undertakes the addressing of envelopes and the despatch of notices of local Meetings.

VII. FINANCE.

1. *Cost of Publications.* Increased charges for printing and an increase in the price of paper have had to be met during the year. This has inevitably led to an increase in the cost per page of the *Journal* and of *British Abstracts*. To help meet this expenditure, the Society has benefited from the increase in the schedule price of publications, which came into force at the beginning of the year.

2. *Contributions.* The Council gratefully acknowledges the sum of £4500 received through the Royal Society from the Government Scientific Publications Grant-in-Aid, and the sum of £10,000 received from the Chemical Council towards the cost of Publications in 1950. The payment from the Chemical Council was made in order to enable the Society to make grants to the Bureau of Abstracts. The Chemical Council will consider further grants in aid of publications when the Accounts of the various Societies for 1950 are available.

3. *Bureau of Abstracts.* In view of a decision of the Chemical Council that grants will not, in future, be made direct to the Bureau of Abstracts, the Council has agreed to increase the annual grant for 1950 to £10,600, thus doubling the Society's normal Contribution to the Bureau.

4. *Library.* The Council records its thanks for a contribution of £300 received through the Royal Society from the Government Scientific Publications Grant-in-Aid, towards the cost of capital expenditure on the Library and for a grant of £371 11*s.* 7*d.* from the Chemical Council towards maintenance costs.

The thanks of the Council are due for the following contributions on a membership basis, received through the Chemical Council towards the maintenance costs of the Library:

	£	*s.*	*d.*
The Royal Institute of Chemistry	1645	13	2
The Society of Chemical Industry	606	2	4
The Faraday Society	169	6	2
The Society of Public Analysts and Other Analytical Chemists	115	2	7
The Biochemical Society	125	5	8

The Chemical Society's share of the maintenance costs of the Library amounted to £724 12*s.* 7*d.* and, in addition, the Society has contributed £2,725 1*s.* 10*d.* towards the purchase of new books and other capital expenditure on the Library.

The Council also gratefully records its thanks for contributions towards maintenance expenses also received from other sources, as follows:

	£	*s.*	*d.*
The Association of British Chemical Manufacturers	100	0	0
The Institute of Brewing	50	0	0
Genatosan, Ltd.	25	0	0
The Society of Dyers and Colourists	10	10	0

5. *Subscriptions under Covenant.* The Society has encouraged Fellows who pay Income Tax at the full rate to enter into a Deed of Covenant with the Society in respect of their Annual Subscription. In this way the Society can recover the Tax on the gross amount of the Subscription and no additional cost falls upon the Fellow.

Some five hundred Fellows have already signed Covenants, and the Society will be able to reclaim over £900 in Income Tax during 1951.

6. *Sir Gilbert Morgan—Bequest.* As will be seen from the list of Investments given with the Accounts, most of the capital comprising the Corday–Morgan Memorial Fund and

the Corday–Morgan Medal and Prize Fund has now been transferred to the Society by the Public Trustee.

7. *Investments.* The following additions to the Society's Investments have been made during the year :

Centenary Fund. £1700 invested in £1716 15*s.* 2*d.* Northern Ireland 3½% Stock, 1969/71.

Corday–Morgan Medal and Prize Fund. £800 invested in £846 7*s.* 0*d.* 3½% War Loan.

Research Fund. £1080 7*s.* 4*d.*, which includes a further sum of £80 7*s.* 4 received under the W. S. Gilles Bequest, invested in £1116 7*s.* 0*d.* New Zealand 3% Stock, 1973/77.

Special Lectures Fund. £100 invested in £107 19*s.* 0*d.* British Transport 3% Stock; 1978/88.

In addition, £1500 3% Savings Bonds 1955/65 and £1835 2½% Funding Loan 1956/61 have been transferred from Special Reserve Fund to the Research Fund in order to repay the sum of £3350 accumulated during the War years and held temporarily in the Special Reserve Fund.

VIII. RELATIONS WITH OTHER BODIES

1. REPRESENTATIVES OF THE SOCIETY ON OTHER BODIES.

Association of British Chemical Manufacturers :

Joint Technical Committee on Patents : Dr. J. T. Hewitt.

Barker Committee :

Formed to support the publication of the Barker Index of the characteristic angles of crystalline compounds : Dr. G. M. Bennett.

Bristol University Court :

Professor T. S. Moore.

British National Committee for Chemistry :

Professor D. H. Hey, Sir Cyril Hinshelwood, Professor M. Stacey.

British National Committee for Crystallography :

Dr. G. M. Bennett.

British Standards Institution. Technical Committees :

M/1.	Units and Technical Data : The Editor.
M/4.	Letter Symbols : The Editor.
C/17.	Viscosity : Dr. A. E. Dunstan.
C/18.	Chemical Symbols and Abbreviations : The Editor.
C/34.	Standardisation of pH Scale : Professor H. T. S. Britton.
CHE/36.	Chemicals for Electroplating : Dr. U. R. Evans.
DAC/-.	Standards for Dairying Chemistry : Mr. Eric Voelker.
LBC/-.	Scientific Glassware and Related Laboratory Apparatus : Dr. G. R. Davies.
LBC/2/1.	Ubbelohde Apparatus : Dr. G. R. Davies.
LBC/5.	Hydrometers : Mr. R. Sutcliffe.
LBC/6.	Standard Distillation Apparatus : Mr. R. Sutcliffe.
LBC/11.	Microchemical Apparatus : Mr. R. Belcher, Dr. H. D. K. Drew.
LGE/19.	Colour Terminology : Dr. F. M. Hamer.
PCC/1.	Nomenclature for Insecticides : Professor R. L. Wain.

Bureau of Abstracts.

Directors and Members: Sir Wallace Akers, Dr. G. M. Bennett, Dr. G. M. Dyson, Professor D. H. Hey.

Members: Mr. R. P. Bell, Dr. A. H. Cook, Dr. H. N. Rydon, Professor W. Wardlaw.

Chemical Council:

The Treasurer, Professor H. Burton, Sir Ian Heilbron, Professor D. H. Hey.

City and Guilds of London Institute:

The President.

Faraday Society. Colloidal and Biophysics Committee:

Dr. P. Johnson.

Joint Library Committee:

Dr. J. H. Burgoyne, Dr. A. H. Cook, Dr. F. Fairbrother, Dr. J. E. Garside, Dr. P. Haas, Dr. J. R. I. Hepburn, Professor D. H. Hey, Professor E. D. Hughes, Dr. Harold King, Professor G. A. R. Kon, Dr. H. N. Rydon, Dr. F. C. Tompkins, Professor C. Tyler, Dr. J. Walker.

Lawes Agricultural Trust:

Committee of Management: Sir John Simonsen.

Parliamentary and Scientific Committee:

Sir Ian Heilbron, Professor H. Burton.

Regional Council for Further Education for the South-West:

Chemistry and Chemical Technology Committee: Professor W. E. Garner.

Royal Society: Joint Standing Committee for Symbols and Abbreviations: Mr. R. P. Bell, The Editor.

Royal Society: Scientific Societies Accommodation Committee:
Sir Ian Heilbron.

Yorkshire Council for Further Education:

Advisory Committee for Chemistry in South and East Yorkshire: Professor R. D. Haworth.

2. REPRESENTATIVES OF THE SOCIETY AT PUBLIC FUNCTIONS.

50th Anniversary of the Discovery of the Grignard Reagent, Lyons, May 13th: Professor H. Burton and Professor D. H. Hey.

50th Anniversary of the Discovery of Radium, Paris, July 16th–20th: Professor F. A. Paneth.

5th International Congress of Microbiology, Rio de Janeiro, August 17th–24th: Mr. W. J. Weir.

Ramsay Chemical Dinner, Glasgow, December 15th: The President.

University of Birmingham—Jubilee Celebrations, May 4th–5th: Professor W. Wardlaw.

APPENDIX A.

MEETINGS HELD DURING 1950.

IN LONDON.

Unless otherwise stated all meetings were held in the Rooms of the Society at Burlington House.

January 19th, at the Royal Institution, *Tilden Lecture*, "Studies on Electron-transfer Reactions", by Professor M. G. Evans; February 2nd, *Meeting* for reading of papers; February 16th, at the Institution of Mechanical Engineers, *Pedler Lecture*, "Polycyclic Aromatic Hydrocarbons", by Professor J. W. Cook; March 2nd, at the Imperial College of Science and Technology, *Centenary Lecture*, "The Azulenes", by Professor Dr. Pl. A. Plattner (Zurich); March 16th, *Meeting* for reading of papers; May 4th, at the Royal Institution, *Tilden Lecture*, "Recent Advances in the Chemistry of the Steroids", by Professor F. S. Spring; June 1st, *Meeting* for reading of papers; October 12th, *Meeting* for reading of papers; November 2nd, *Symposium*, "Tropolones and Allied Compounds", introduced by Professor J. W. Cook; November 16th, *Meeting* for reading of papers; December 14th, *Meeting* for reading of papers.

OUTSIDE LONDON.

Aberdeen. Joint meetings with the local sections of the Royal Institute of Chemistry and the Society of Chemical Industry, in the Chemistry Department, Marischal College: January 8th, *Lecture*, "The Deflocculation of Long-fibred Pulps by Natural Mucilages", by Dr. H. Ainsworth Harrison; February 16th, *Lecture*, "Applications of Exothermic Solid Reactions to Jet Propulsion and Industrial Purposes", by Dr. James Taylor; March 9th, *Lecture*, "The Chemistry of Anæsthetics", by Professor H. B. Nisbet; October 20th, *Lecture*, "Recent Work on the Transuranic Elements", by Dr. R. Hurst; November 7th, *Lecture*, "Some Aspects of the Chemistry of Polycyclic Aromatic Hydrocarbons", by Professor J. W. Cook; December 1st, *Lecture*, "Instrumentation in Modern Methods of Analysis", by Mr. E. J. Vaughan.

Birmingham. At the University: January 20th (joint meeting with the University Chemical Society), *Lecture*, "The Separation and Determination of the Sugars and their Derivatives", by Dr. J. K. N. Jones; February 10th, Official Meeting of the Society and *Lecture*, "Fifty Years of Organic Chemistry", by Sir Ian Heilbron; March 17th, *Lecture*, "How Crystals Grow", by Professor E. K. Rideal; (joint meetings with the University Chemical Society): May 12th, *Lecture*, "The Shape of a Chemical Bond", by Professor C. A. Coulson; October 20th, *Lecture*, "Chemistry and the Scattering of Light", by Dr. E. J. Bowen; December 8th, *Lecture*, "Homolytic Aromatic Substitution", by Professor D. H. Hey.

Bristol. (Joint meetings with the local sections of the Royal Institute of Chemistry and the Society of Chemical Industry), at the University: February 9th, *Lecture*, "Studies of some Organic Fluorine Compounds", by Professor M. Stacey; October 12th, *Lecture*, "The Changing Face of Chemical Industry", by Dr. A. C. Monkhouse; November 2nd, *Lecture*, "The Hahn Emanation Technique", by Dr. J. S. Anderson; November 24th, at Gloucester Technical College, *Lecture*, "The Manufacture of Nitric Acid", by Mr. C. Wilson; at the University: November 23rd, *Lecture*, "Cereal Chemistry", by Dr. D. W. Kent-Jones; December 7th, *Lecture*, "Carbon as a Material of Construction", by Mr. A. W. Morrison.

Edinburgh. (Joint meetings with the local sections of the Royal Institute of Chemistry and the Society of Chemical Industry): January 19th, at the North British Station Hotel, *Lecture*, "The Deflocculation of Long-fibred Pulps by Mucilages", by Dr. H. Ainsworth Harrison; February 7th, at the University (with the University Chemical Society), *Lecture*, "Some Aspects of Solid Reactions", by Professor W. E. Garner; at the North British Station Hotel: February 23rd, *Lecture*, "The Planning of Semi-technical-Scale Experiments", by Dr. R. Holroyd; March 16th, *Lecture*, "Some Aspects of Photo-oxidation with Reference to Chlorophyll", by Dr. M. Ritchie; October 26th, *Lecture*, "The Scientific Examination of Pictures", by Dr. A. E. Werner; November 23rd, *Lecture*,

" Homolytic Aromatic Substitution ", by Professor D. H. Hey; December 14th, *Lecture*, " Modern Trends in Fuels and Lubricants ", by Dr. E. M. Dodds.

Exeter. At the Washington Singer Laboratories: May 2nd, *Lecture*, " Some Aspects of Aromatic Substitution ", by Professor Brynmor Jones; October 13th (joint meeting with University College Chemical Club), *Lecture*, " Research in the Paint Industry ", by Dr. J. W. Dorling; October 20th, at the Technical College, Plymouth (joint meeting with the local sections of the Royal Institute of Chemistry and the Society of Chemical Industry), *Lecture*, " The Basic Principles of Chemical Engineering ", by Mr. M. B. Donald; at the Washington Singer Laboratories: November 10th, *Lecture*, " Editing for the Chemical Society ", by Dr. R. S. Cahn; December 1st (joint meeting with the local sections of the Royal Institute of Chemistry and the Society of Chemical Industry), *Lecture*, " Some Scientific Aspects of Pulp and Paper Manufacture ", by Dr. J. Grant.

Glasgow. At the Royal Technical College: January 27th, *Lecture*, " Recent Advances in the Chemistry of the Steroids ", by Professor F. S. Spring; February 24th, Annual General Meeting and *Meeting* for reading of papers; at the University: March 10th, *Lecture*, " Purine Synthesis—A New Chapter ", by Dr. A. H. Cook; October 25th, at the Royal Technical College (joint meeting with the Alchemists' Club of the University and the Andersonian Chemical Society of the Royal Technical College), *Lecture*, " Recent Developments in Macrocyclic Pigments ", by Professor R. P. Linstead; November 17th, at the University, *Lecture*, " Some Problems in Gas Flow and Sorption ", by Professor R. M. Barrer; December 1st, at the Beresford Hotel, *Ramsay Chemical Dinner*; December 15th, at Ardeer (joint meeting with the Ardeer Chemical Club and the local sections of the Royal Institute of Chemistry and the Society of Chemical Industry), *Lecture*, " Cortisone ", by The Right Hon. the Earl of Halsbury.

Hull. At University College: (joint meetings with University College Scientific Society), January 19th, *Lecture*, " Modern Trends in Stereochemistry ", by Professor E. E. Turner; February 9th, *Lecture*, " Some Recent Applications of Infra-red Spectroscopy ", by Dr. H. W. Thompson; March 2nd (joint meeting with the local section of the Royal Institute of Chemistry), *Lecture*, " Aromatic Nitration ", by Dr. G. M. Bennett; (joint meetings with University College Scientific Society): November 16th, *Lecture*, " Recent Theories of Molecular Structure ", by Sir John Lennard-Jones; December 8th, *Lecture*, " Chemical Personalities a Century Ago ", by Professor John Read.

Irish Republic. At University College, Dublin: January 11th, *Lecture*, " Cortisone Problem ", by Professor E. R. H. Jones; [joint meetings with the Irish Chemical Association, the Royal Institute of Chemistry (Dublin Section), and the Society of Chemical Industry (Dublin Section)]: March 1st, *Lecture*, " Deoxy-sugars and Nucleic Acids ", by Professor M. Stacey; March 3rd, at University College, Cork, *Lecture*, " Bacterial Nucleic Acids ", by Professor M. Stacey; March 6th, at University College, Galway, *Lecture*, " Deoxy-sugars and Nucleic Acids ", by Professor M. Stacey; March 8th, at Trinity College, Dublin, *Lecture*, " Lycomarasmin: The Chemistry of Wilting Diseases ", by Professor Dr. Pl. A. Plattner; May 23rd, at University College, Dublin (Joint meeting with University College Chemical Society), *Lecture*, " Some Problems in Polysaccharide Chemistry ", by Dr. E. G. V. Percival; at Trinity College, Dublin: October 25th, *Lecture*, " Editing for the Chemical Society ", by Dr. R. S. Cahn; November 10th (joint meeting with the Werner Society), *Lecture*, " The Degradation of High Polymers ", by Professor H. W. Melville.

Leeds. At the University: January 30th, *Lecture*, " The Basis of Chemotherapeutic Research ", by Dr. F. L. Rose; February 21st (joint meeting with the University Chemical Society), *Lecture*, " Some Recent Applications of Dipole-moment Measurements to Molecular Structure ", by Professor H. D. Springall.

Liverpool. At the University: (joint meetings with the British Association of Chemists and the local sections of the Royal Institute of Chemistry and the Society of Chemical Industry): March 7th, *Lecture*, " Lycomarasmin. The Chemistry of Wilting Diseases ", by Professor Dr. Pl. A. Plattner; March 16th, *Lecture*, " Heterogeneous Catalysis ", by Professor E. K. Rideal; March 23rd, *Lecture*, " Photo-excited Electron-transfer Reactions ", by Professor M. G. Evans; November 9th, *Lecture*, " Polymerisation and its

Reversal", by Professor F. S. Dainton; November 23rd, *Lecture*, "The Chemistry of Tropolone and Some of its Derivatives", by Professor R. D. Haworth.

Manchester. At the University: January 19th (joint meeting with the local sections of the Royal Institute of Chemistry and the Society of Chemical Industry), *Lecture*, "Localised and Non-localised Bonds", by Professor C. A. Coulson; February 16th, *Meeting* for the reading of papers; February 23rd, at the Engineer's Club (joint meeting with the local sections of the Royal Institute of Chemistry and the Society of Chemical Industry), *Lecture*, "Research in Progress in the Organic Chemistry Department of Manchester University", by Professor E. R. H. Jones; at the University: March 3rd, *Lecture*, "The Azulenes", by Professor Dr. Pl. A. Plattner; March 9th, *Pedler Lecture*, "Polycyclic Aromatic Hydrocarbons", by Professor J. W. Cook; March 22nd, at the Engineer's Club (joint meeting with the local sections of the Royal Institute of Chemistry and the Society of Chemical Industry), *Lecture*, "Some Recent Applications of Infra-red Spectroscopy", by Dr. H. W. Thompson; at the University (joint meetings with the local sections of the Royal Institute of Chemistry and the Society of Chemical Industry); October 19th, Official Meeting and *Lecture*, "The Chemistry of the Tropolones", by Professor R. D. Haworth; November 8th, *Lecture*, "Catalysed Oxidation", by Professor C. E. H. Bawn; December 1st, at the College of Technology, *Lecture*, "The Application of Radioactive Isotopes in Industry", by Mr. K. Fearnside; at the University, December 14th, *Meeting* for reading of papers.

Newcastle and Durham. At King's College, Newcastle-on-Tyne: November 10th, *Bedson Club Lecture*, "Resonance Transfer of Energy between Molecules", by Dr. E. J. Bowen; November 24th, *Meeting* for reading of papers; December 8th, *Bedson Club Lecture*, "The Application of Halogen Fluorides in Preparative Inorganic Chemistry", by Professor H. J. Emeléus. Fellows were invited to the meetings of the Bedson Club.

Northern Ireland. At Belfast: January 20th (joint meeting with the local sections of the Royal Institute of Chemistry and the Society of Chemical Industry), *Lecture*, "Chemical Education", by Mr. J. McG. Jackson; February 8th (joint meeting with the local sections of the Royal Institute of Chemistry, the Society of Chemical Industry, and the Society of Dyers and Colourists), *Lecture*, "Colours in Food", by Mr. E. R. Eaton; (joint meetings with the local sections of the Royal Institute of Chemistry and the Society of Chemical Industry); March 10th, *Lecture*, "Inorganic Chromatography", by Mr. R. A. Wells; September 21st, *Lecture*, "A Review of Methods for Determining Moisture in Organic Materials", by Dr. M. H. Hall; (joint meetings with the Andrews Club, the local sections of the Royal Institute of Chemistry, and the Society of Chemical Industry): November 14th, *Lecture*, "Some Problems in the Chemistry of the Polysaccharides", by Professor E. L. Hirst; November 28th, *Lecture*, "Some Aspects of Cellulose Autoxidation", by Dr. D. Entwhistle.

North Wales. (*a*) At University College of North Wales, Bangor. (Joint meetings with the University College of North Wales Chemical Society): February 2nd, *Lecture*, "Some Aspects of the Chemistry of Simple Peptides", by Professor F. E. King; May 4th, *Lecture*, "Light-scattering and Chemistry", by Dr. E. J. Bowen; October 13th, *Lecture*, "Studies in the Synthesis of Flavones", by Professor T. S. Wheeler; Official Meeting and *Tilden Lecture*: November 23rd, "A Chemotherapeutic Search in Retrospect", by Dr. F. L. Rose.

(*b*) At the Edward Davies Chemical Laboratories, Aberystwyth (joint meetings with the University College of Wales Chemical Society); March 9th, *Lecture*, "Some Recent Developments in the Chemistry of Indole Derivatives", by Dr. R. J. S. Beer; October 19th, *Lecture*, "Polyacetylenes", by Professor E. R. H. Jones.

Nottingham. At the University (joint meetings with the University Chemical Society): February 23rd, *Lecture*, "Synthesis in the Nucleotide Field", by Professor A. R. Todd; March 9th, *Lecture* "Some Aspects of Structural Chemistry", by Professor W. Wardlaw; March 16th, *Lecture*, "Microwave Spectroscopy", by Professor E. Bright Wilson, jun.; October 19th, *Lecture*, "Hydrogen Peroxide as an Ionising Solvent", by Professor W. F. K. Wynne-Jones; November 2nd, *Lecture*, "The Cortisone Problem", by Professor C. W. Shoppee; November 9th, *Lecture*, "Recent Chemical Applications of Electric Dipole-moment Measurements", by Dr. L. E. Sutton.

Oxford. Fellows were invited to the following *Alembic Club Lectures* held at the Physical

Chemistry Laboratory: January 30th, *Lecture*, "Some Recent Developments in Acetylene Chemistry", by Professor E. R. H. Jones; February 6th (joint meeting with the Royal Institute of Chemistry), *Lecture*, "Analytical Chemistry: Science or Art", by Dr. H. M. N. H. Irving; February 27th, *Lecture*, "Some Unifying Concepts in Chemistry", by Sir John Lennard-Jones; May 1st, *Lecture*, "The Biochemistry of Fluoroacetate Poisoning and its Significance", by Professor R. A. Peters; May 15th, *Lecture*, "Some Problems in the Chemistry of Starch and Glycogen", by Professor E. L. Hirst; June 5th, *Lecture*, "Catalysis on Oxides", by Professor W. E. Garner; October 23rd, *Lecture*, "Dielectric Constants of Solutions", by Professor E. A. Guggenheim; November 6th, *Lecture*, "Phthalocyanines and Porphyrins", by Professor R. P. Linstead; November 20th, *Lecture*, "Neutron Diffraction", by Professor K. Lonsdale.

St. Andrews and Dundee. At University College, Dundee: January 12th, *Lecture*, "Keto-enol Equilibrium", by Mr. R. P. Bell; February 2nd (joint meeting with the British Association Dundee Trust), *Lecture*, "The Concept of Nature from Copernicus to Newton", by Sir Edmund Whittaker; April 6th, *Lecture*, "Chemical Reactions induced by Nuclear Radiations", by Professor F. S. Dainton; April 7th, at United College, St. Andrews (joint meeting with St. Andrews University Chemical Society), *Lecture*, "Developments in the Chemistry of *cyclo*Heptane Derivatives", by Professor R. D. Haworth; at United College, St. Andrews: (joint meetings with St. Andrews University Chemical Society); October 20th, *Lecture*, "Historical Science as an Instrument of Culture", by Professor J. Read; November 3rd, *Lecture*, "Chemical Aspects of the Cell Nucleus", by Professor J. N. Davidson; November 10th (joint meeting with the local section of the Royal Institute of Chemistry), *Lecture*, "Bond Lengths, their Measurement and their Significance", by Professor E. G. Cox; (joint meetings with St. Andrews University Chemical Society): November 24th, *Lecture*, "Homolytic Aromatic Substitution", by Professor D. H. Hey; December 1st, *Lecture*, "Micro-techniques in Chemistry", by Dr. A. F. Colson.

Sheffield. At the University: February 9th (joint meeting with the University Chemical Society), *Lecture*, "The Breakdown of High Polymers", by Professor H. W. Melville; March 9th (joint meeting with the local section of the Royal Institute of Chemistry, *Lecture*, "The Treatment of Water for Industrial Purposes", by Mr. P. Hamer; (joint meetings with the University Chemical Society): March 16th, *Lecture*, "Recent Developments in Acetylene Chemistry", by Professor E. R. H. Jones; April 27th, *Tilden Lecture*, "Recent Advances in the Chemistry of the Steroids", by Professor F. S. Spring; November 9th (joint meeting with the local section of the Royal Institute of Chemistry), *Lecture*, "Hydrocarbons as Raw Materials for Organic Chemical Industry", by Dr. R. J. Holroyd; November 30th (joint meeting with the University Chemical Society), *Lecture*, "New Ventures in Carbohydrate Chemistry", by Professor M. Stacey.

Southampton. At University College (joint meetings with the University College Chemical Society): February 17th, *Lecture*, "Modern Inorganic Stereochemistry", by Mr. R. S. Nyholm; March 3rd, *Lecture*, "The Determination of Traces of Elements and Compounds", by Dr. H. M. N. H. Irving; April 26th, at Portsmouth Municipal College (joint meeting with Mid-Southern Counties Section of the Royal Institute of Chemistry and Portsmouth and District Chemical Society), *Lecture*, "Trace-elements in Plant Life," by Dr. W. A. Roach; May 5th, at University College (joint meeting with the University College Chemical Society), *Lecture*, "Recent Synthetical Developments in Pyrethrum Chemistry", by Dr. S. H. Harper; October 9th, at Portsmouth Municipal College (joint meeting with the Mid-Southern Counties Section of the Royal Institute of Chemistry and the Portsmouth and District Chemical Society), *Lecture*, "The New Elements", by Professor H. J. Emeléus; at University College: October 20th (joint meeting with the University College Chemical Society and the Mid-Southern Counties section of the Royal Institute of Chemistry), *Lecture*, "Mediaeval Chemical Industries", by Dr. F. Sherwood Taylor; November 17th (Joint meeting with University College Chemical Society), Official Meeting and *Lecture*, "Kinetics of the Bacterial Cell", by Sir Cyril Hinshelwood.

South Wales. At University College, Swansea: February 10th (joint meeting with the University College of Swansea Students' Chemical Society and the local section of the

Royal Institute of Chemistry), *Lecture*, "Some Problems in Inorganic Chemistry", by Professor W. Wardlaw; March 3rd (joint meeting with the University College of Swansea Students' Chemical Society), *Lecture*, "Synthetical Investigations in the Series of Cyclic Imines", by Professor F. E. King; (joint meetings with the University College of Swansea Chemical Society and the local section of the Royal Institute of Chemistry): October 13th, *Lecture*, "Some Aspects of the Chemistry of Sulphur Compounds occurring in Nature", by Professor F. Challenger; November 17th, *Lecture*, "Ion-exchange Resins", by Professor C. W. Davies.

APPENDIX B.

ANNUAL REPORT OF THE JOINT LIBRARY COMMITTEE FOR THE YEAR 1950.

The fact that most of the figures relating to the activities of the Library for 1950 show a decrease compared with those for the previous year suggests that the work of the Library has decreased. This, however, is not so, as the accommodation in the Reading Room is frequently severely taxed and the increasing dispersal of books throughout the building adds considerably to the work of the staff. A good deal of headway has been made in catching up arrears of binding which accumulated during the war.

The number of printed pages of which photostat copies were made during 1950 was 3952, compared with 5018 in 1949. The telephone enquiries number 2377, an increase of 392 over the previous year. A total of 422 books was added to the Library, of which 124 were presented. The number of volumes of periodicals added reached 898, and there were also 233 pamphlets received. The total number of volumes in the Library would have reached 51,999, but 425 volumes of periodicals which are outside the present scope of the Library were disposed of for the benefit of needy libraries, so the actual total is 51,574, of which 15,795 are books and 35,779 volumes of periodicals.

	Attendances.	Books borrowed.	Additions: Books.	Additions: Volumes of periodicals.	Additions: Pamphlets.
1950	10,415	8294 (3284 by post)	422	898	233
1949	10,778	8926 (4177 by post)	319	573	224

An Edison–Swan Microfilm Reader has been purchased for use in the Library to replace the Spencer Reader, and this has proved a great advantage to readers wishing to consult microfilms.

It is gratifying to note that nearly twice as many books were presented to the Library in 1950 as in the previous year. These range from photostat copies of extremely rare books to newly published items. The Committee is most grateful to all those who have shown their appreciation of the Library in this way.

INCOME AND EXPENDITURE GENERAL PURPOSES ACCOUNT FOR THE YEAR ENDED 31ST DECEMBER, 1950.

1949 £ s. d.	1949 £ s. d.	*Income.*	1950 £ s. d.	1950 £ s. d.
	23 5 0	To Life Composition Fees		71 16 8
		,, Annual Subscriptions :		
		Single-body Fellows—		
4260 2 4		Received in advance, on account of 1950	5516 12 0	
5906 19 8		Received during 1950 on account of 1950	7068 10 8	
245 16 3		Received during 1950 on account of 1949 and previous years	373 5 3	
		Joint Fellows—		
380 10 2		Received in advance on account of 1950	4263 2 6	
11,374 19 3		Received during 1950 on account of 1950	8885 14 6	
128 12 0		Received during 1950 on account of 1949 and previous years	140 16 4	
22,296 19 8			26,248 1 3	
		Less Amount included in last year's Income, being valuation of Arrears as per last Balance Sheet	300 0 0	
21,996 19 8			25,948 1 3	
300 0 0		*Add* Arrears to date estimated to realise as per Balance Sheet ...	300 0 0	
22,296 19 8			26,248 1 3	
332 0 0		*Add* Adjustment of cost of publications supplied to Joint Members	633 0 0	
	22,628 19 8			26,881 1 3
	594 0 11	,, Dividends on Investments		882 19 3
	300 9 10	,, Income Tax recovered		185 19 8
	91 18 2	,, Donations		90 18 2
	101 9 5	,, Miscellaneous Receipts		180 15 4
		,, Balance, being Excess of Expenditure over Income, carried to Balance Sheet		
	111 4 5			207 4 8
	£23,851 7 5			£28,500 15 0

1949 £ s. d.	1949 £ s. d.	*Expenditure.*	1950 £ s. d.	1950 £ s. d.
		By Administration Expenses :		
4204 9 1		Office Salaries and Wages	4184 5 4	
461 19 10		Superannuation	471 17 3	
1126 11 0		House Expenses, etc.	913 5 2	
117 12 0		Accountants' Charges	180 12 0	
817 0 2		Printing, Stationery, and Office Expenses	939 17 9	
290 10 3		Postages	291 12 3	
205 16 0		Furniture	145 4 6	
268 8 3		Miscellaneous	341 5 8	
	7492 6 7			7467 17 11
		,, Expenses on Account of Conjoint Chemical Office		1111 2 9
	1400 0 0	,, Expenses of Meetings		784 14 10
	411 16 6	,, Donations		81 10 0
	31 10 0	,, Balance of Expenditure on Publications to Publications Account		
	11,810 4 4			14,560 14 7
		,, Contribution to Library Account :		
943 6 9		For Fittings, Furniture, Books, Periodicals, and Binding	2735 1 10	
618 7 6		Proportion of Maintenance	734 12 7	
	1561 14 3			3469 14 5
	300 0 0	,, Transfer to Staff Pensions Fund		300 0 0
	296 17 6	,, Expenses of Local Representatives		463 19 10
	21 10 0	,, Legal Charges		— — —
	240 16 9	,, Travelling Expenses of Members of Council		861 0 8
	84 11 6	,, Loss on Exchange (Australia)		— — —
	£23,851 7 5			£28,500 15 0

INCOME AND EXPENDITURE ACCOUNTS OF OTHER FUNDS FOR THE YEAR ENDED 31ST DECEMBER, 1950.

PUBLICATIONS.

1949 £ s. d.	1949 £ s. d.	*Income.*	1950 £ s. d.	1950 £ s. d.
		To Publication Sales (including back numbers):		
8793 5 6		Journals and Proceedings	11,914 7 6	
1447 19 4		Annual Reports on Progress of Chemistry	1825 17 4	
1364 10 8		Quarterly Reviews	1470 17 7	
1766 16 6		Authors' Extra Reprints	1409 19 9	
392 14 2		Abstracts (Back Nos. only 1944 and earlier)	156 19 4	
12 3 8		Other Publications	5 12 9	
	13,777 9 10			16,783 14 3
		„ Net Proceeds of Advertisements:		
784 13 7		Journal	883 19 1	
46 5 11		Quarterly Reviews	91 5 5	
73 15 11		Annual Reports	57 7 2	
	906 15 5			1032 11 8
		„ Donations:		
2333 6 8		The Chemical Council	10,000 0 0	
		The Chemical Council (for British Abstracts, AIII)	1483 18 4	
	2333 6 8			11,483 18 4
	2900 0 0	„ Government Publications Grant (through the Royal Society)		4500 0 0
		„ Cost of publishing Tilden Lectures:		
	25 4 0	Transfer from the Tilden Lecture Fund		— — —
		„ Cost of publishing Centenary Lectures:		
	50 0 0	Transfer from the Centenary Fund		— — —
	736 16 2	„ Donations		1 11 0
	196 5 6	„ Dividends on Investments		567 14 0
	133 5 6	„ Income Tax recovered		82 14 6
	9000 0 0	„ Transfer from Special Reserve Fund		— — —
	6 12 7	„ Miscellaneous Receipts		— — —
		„ Transfer from General Purposes Account (the balance of expenditure on publications)		14,860 14 7
	11,810 4 4			
	£41,876 18 0			£48,812 18 4

1949 £ s. d.	1949 £ s. d.	*Expenditure.*	1950 £ s. d.	1950 £ s. d.
		By Expenses on account of Journal:		
3635 11 11		Salaries and Wages	4063 9 2	
335 6 5		Superannuation	367 1 4	
21,098 19 6		Printing and Paper	20,026 6 6	
2050 2 6		Binding and Distribution	3264 13 3	
3093 15 3		Authors' Reprints	2504 11 7	
100 0 0		Indexing	100 0 0	
62 0 3		Furniture	405 9 9	
154 0 6		Office Printing and Stationery	291 3 9	
139 4 5		Editorial Postages	147 12 9	
302 6 2		Miscellaneous	442 19 7	
	31,963 6 5			31,713 7 8
		„ Contributions to Bureau of Abstracts:		
5300 0 0		Grants	10,600 0 0	
		Grant (British Abstracts AIII through the Chemical Council)	1483 18 4	
	5300 0 0			12,083 18 4
	2154 16 8	„ Annual Reports on the Progress of Chemistry		2211 6 1
	2457 14 11	„ Quarterly Reviews		2804 6 5
	£41,876 18 0			£48,812 18 4

INCOME AND EXPENDITURE ACCOUNTS OF OTHER FUNDS FOR THE YEAR ENDED 31ST DECEMBER, 1950.

LIBRARY.

1949			*Income.*	1950		
£ s. d.	£ s. d.			£ s. d.	£ s. d.	
			To Contributions for Fittings, Furniture, Books, Periodicals, and Binding:			
943 6 9			Transfer from General Purposes Account ...	2725 1 10		
200 0 0			„ Government Grant (through the Royal Society)	300 0 0		
	1143 6 9				3025 1 10	
			„ Contributions towards maintenance:			
			Through the Chemical Council:			
			Chemical Society (transfer from General Purposes Account)	724 12 7		
618 7 6			Royal Institute of Chemistry	1645 13 2		
1188 19 4			Society of Chemical Industry	606 2 4		
638 1 0			Faraday Society	169 6 2		
132 2 2			Society of Public Analysts and other Analytical Chemists	115 2 7		
101 5 9			Biochemical Society	125 5 8		
132 2 2			From the Chemical Council	371 11 7		
825 6 7						
	3636 2 6				3757 14 1	
			„ Contributions, etc., received from other sources towards maintenance:			
			Association of British Chemical Manufacturers	100 0 0		
100 0 0			Institute of Brewing	50 0 0		
50 0 0			Society of Dyers and Colourists	10 10 0		
10 10 0			Miscellaneous receipts	54 6 0		
60 10 5						
	221 0 5				214 16 0	
	£5000 9 8				£6997 11 11	

1949			*Expenditure.*	1950		
£ s. d.	£ s. d.			£ s. d.	£ s. d.	
			By Capital and Extraordinary Expenditure:			
870 10 6			Books and Periodicals *	1307 0 11		
34 6 9			Furniture	73 12 6		
238 9 6			Binding	1644 8 5		
	1143 6 9				3025 1 10	
			Maintenance:			
3049 8 7			Salaries and Wages	3017 14 2		
277 2 10			Superannuation of Library Staff	288 6 4		
65 11 4			Postages	77 9 7		
199 0 6			House Expenses, etc.	336 13 3		
131 15 9			Office Expenses and Stationery	146 17 9		
134 3 11			Miscellaneous Expenses	105 10 0		
	3857 2 11				3972 10 1	
	£5000 9 8				£6997 11 11	

* Other than those received in exchange.

Income and Expenditure Accounts of other Funds for the Year ended 31st December, 1950.

SPECIAL RESERVE FUND.

1949			*Income.*				1949			*Expenditure.*			
£	s.	d.		£	s.	d.	£	s.	d.		£	s.	d.
320	1	7	To Dividends on Investments	306	2	2				By Balance, being Excess of Income over Expenditure, carried to Balance			
14	2	9	„ Interest on Deposit	8	12	6	431	5	5	Sheet	386	12	2
97	1	1	„ Income Tax recovered	71	17	6							
£431	5	5		£386	12	2	£431	5	5		£386	12	2

RESEARCH FUND.

£	s.	d.		£	s.	d.	£	s.	d.		£	s.	d.
350	15	0	TO Dividends on Investments	625	8	10	775	2	0	By Grants awarded	877	15	0
256	2	7	„ Income Tax recovered	137	6	11	20	0	0	„ Honorarium, Longstaff Medallist			
35	13	8	„ Repayment of Grants	35	15	2	34	19	4	„ Miscellaneous Expenses	41	6	9
3	7	1	„ Interest on Deposit	3	0	0							
2	10	0	„ Sale of Apparatus	—	—	—							
70	0	0	„ Grants not claimed	37	16	8							
			„ Balance, being Excess of Expenditure over Income, carried to Balance										
111	13	0	Sheet	79	14	2							
£830	1	4		£919	1	9	£830	1	4		£919	1	9

SPECIAL PUBLICATIONS FUND.

£	s.	d.		£	s.	d.	£	s.	d.		£	s.	d.
35	1	2	To Sales of Publications	30	1	11	502	8	11	By Cost of Publications	—	—	—
28	9	2	„ Dividends on Investments	69	18	2	6	6	9	„ Miscellaneous Expenses	6	10	0
26	9	4	„ Income Tax recovered	15	14	6				„ Balance, being Excess of Income over Expenditure, carried to Balance			
26	15	9	„ Interest on Deposit	14	7	0	—	—	—	Sheet	123	11	7
362	1	3	„ Balance, being Excess of Expenditure over Income, carried to Balance Sheet	—	—	—							
£508	15	8		£130	1	7	£508	15	8		£130	1	7

Income and Expenditure Accounts of other Funds for the Year ended 31st December, 1950.

STAFF PENSIONS FUND.

1949	*Income.*	1950	1949	*Expenditure.*	1950
£ s. d.		£ s. d.	£ s. d.		£ s. d.
500 0 0	To Transfer from General Account	500 0 0	965 0 0	By Pensions	965 0 0
91 3 7	„ Dividends on Investments	95 14 4	6 14 3	„ Miscellaneous Expenses	5 11 6
31 14 9	„ Income Tax recovered	4 11 8			
11 9 1	„ Interest on Deposit	11 3 6			
537 7 10	„ Balance, being Excess of Expenditure over Income, carried to Balance Sheet	559 2 0			
£971 14 3		£970 11 6	£971 14 3		£970 11 6

THE EDWARD FRANK HARRISON MEMORIAL TRUST FUND.

£ s. d.		£ s. d.	£ s. d.		£ s. d.
26 14 10	To Dividends on Investments	46 16 10	— — —	By Plaque	15 15 0
20 2 0	„ Income Tax recovered	10 1 0	2 6 10	„ Miscellaneous Expenses	14 6 11
				„ Balance, being Excess of Income over Expenditure, carried to Balance Sheet	26 15 11
			44 10 0		
£46 16 10		£56 17 10	£46 16 10		£56 17 10

SPECIAL LECTURES FUND.

£ s. d.		£ s. d.	£ s. d.		£ s. d.
24 11 3	To Dividend on Investment	46 17 0	— — —	By Honorarium	25 0 0
9 10 11	„ Income Tax recovered	10 10 9	1 14 4	„ Miscellaneous Expenses	2 17 4
4 11	„ Interest on Deposit	— — —		„ Balance, being Excess of Income over Expenditure, carried to Balance Sheet	29 10 5
			32 12 9		
£34 7 1		£57 7 9	£34 7 1		£57 7 9

Income and Expenditure Accounts of other Funds for the Year ended 31st December, 1950.

THE FARADAY LECTURE FUND.

1949	*Income.*	1950	1949	*Expenditure.*	1950
£ s. d.		£ s. d.	£ s. d.		£ s. d.
7 17 1	To Dividend on Investment	15 8 8	— — —	By Honorarium	25 0 0
5 18 0	„ Income Tax recovered	3 9 8	— — —	„ Faraday Medal	3 17 10
1 11	„ Interest on Deposit	— — —	13 9	„ Miscellaneous Expenses	1 0 8
— — —	„ Balance, being Excess of Expenditure over Income, carried to Balance Sheet	11 0 2		„ Balance, being Excess of Income over Expenditure, carried to Balance Sheet	— — —
£13 17 0		£29 18 8	£13 17 0		£29 18 8

THE TILDEN LECTURE FUND.

1949		1950	1949		1950
£ s. d.		£ s. d.	£ s. d.		£ s. d.
37 3 0	To Dividends on Investments	67 10 8	31 10 0	By Honoraria	— — —
37 11 1	„ Income Tax recovered	19 10 1	36 9 5	„ Lecture Expenses	47 5 0
3 0	„ Interest on Deposit	3 0	23 4 0	„ Transfer to Publications Account, for cost of publication of Lectures	16 9 1
— — —	„ Balance, being Excess of Expenditure over Income, carried to Balance Sheet	— — —	3 4 10	„ Miscellaneous Expenses	— — —
31 11 2			— — —	„ Balance, being Excess of Income over Expenditure, carried to Balance Sheet	7 13 5
£96 8 3		£87 3 9	£96 8 3		15 16 3
					£87 3 9

CENTENARY FUND.

£ s. d.		£ s. d.	£ s. d.		£ s. d.
340 10 0	To Dividends on Investments	329 5 6	337 10 11	By Expenses of Lecturers & Delegates	293 16 1
206 17 8	„ Income Tax recovered	106 4 6	22 7 4	„ Miscellaneous Expenses	38 18 0
— — —			— — —	„ Balance, being Excess of Income over Expenditure, carried to Balance Sheet	— — —
£447 7 8		£435 10 0	87 9 2		302 15 11
			£447 7 8		£435 10 0

INCOME AND EXPENDITURE ACCOUNTS OF OTHER FUNDS FOR THE YEAR ENDED 31ST DECEMBER, 1950.

THE ROBERT JOHN FLINTOFF TRUST.

1949	*Income.*	1950	1949	*Expenditure.*	1950
£ s. d.		£ s. d.	£ s. d.		£ s. d.
3 17 2	To Dividends on Investments	26 9 11		By Miscellaneous Expenses	1 6 6
	„ Interest		3 17 2	„ By Balance, being Excess of Income over Expenditure, carried to Balance Sheet	25 3 5
£3 17 2		£26 9 11	£3 17 2		£26 9 11

THE CORDAY-MORGAN MEMORIAL FUND.

£ s. d.		£ s. d.	£ s. d.		£ s. d.
	To Dividends on Investments	158 19 11		By Memorial Expenses (Clause 12 of the Will)	88 16 6
	„ Interest on Deposit	6 17 7		„ Miscellaneous Expenses	45 8 3
				„ Balance, being Excess of Income over Expenditure, carried to Balance Sheet	61 12 9
		£165 17 6			£165 17 6

THE CORDAY-MORGAN MEDAL AND PRIZE FUND.

£ s. d.		£ s. d.	£ s. d.		£ s. d.
	To Dividends on Investments	98 12 3		By Cost of Medal	7 10 0
	„ Interest on Deposit	12 11		„ Miscellaneous Expenses	24 1 1
				„ Balance, being Excess of Income over Expenditure, carried to Balance Sheet	67 14 1
		£99 5 3			£99 5 3

THE CHEMICAL SOCIETY.—BALANCE SHEETS, 31st December, 1950.

GENERAL PURPOSES.

1949			*Liabilities.*	1950					
£	s.	d.		£	s.	d.	£	s.	d.
			To Sundry Creditors:						
9802	7	8	Fellowship Subscriptions in advance...	6772	7	7			
3221	12	11	Publications sold in advance	3236	16	1			
10,358	13	7	Printing and other Expenses	14,664	6	1			
							26,673	9	9
			„ Excess of Assets over Liabilities as per						
24,090	17	4	last Balance Sheet	24,026	2	11			
46	10	0	*Add* Life Composition Fees	113	13	4			
				24,139	16	3			
24,137	7	4							
111	4	5	*Deduct* Excess of Expenditure over Income for year	207	4	9			
							23,932	11	7
							£50,606	1	4

1949			*Assets.*	1950		
£	s.	d.		£	s.	d.
28,996	12	2	By Investments as per Schedule (cost or value when acquired)	28,996	12	2
10,322	4	2	„ Sundry Debtors	13,678	8	0
200	0	0	„ Subscriptions in Arrear estimated to realise	500	0	0
1416	5	7	„ Stock of Paper (Journal, Annual Reports, and Quarterly Reviews)...	2451	17	0
6373	15	2	„ Cash at Bank and in hand	5179	7	2
£47,408	17	1		£50,606	1	4

THE CHEMICAL SOCIETY. BALANCE SHEETS, 31ST DECEMBER, 1950.

PUBLICATIONS FUND.

1949	*Liabilities.*	1950	1949	*Assets.*	1950
£ s. d.		£ s. d.	£ s. d.		£ s. d.
— — —	To Sundry Creditors	14 14 7	— — —	By Sundry Debtors	14 14 7
9,978 19 7	„ Excess of Assets over Liabilities as per last Balance Sheet	10,978 19 7	10,978 19 7	„ Investments as per Schedule (cost or value when acquired)	10,978 19 7
1,000 0 0	*Add* Legacy—W. H. Perkin	— — —			
£10,978 19 7		10,993 14 2	£10,978 19 7		£10,993 14 2

SPECIAL RESERVE FUND.

£ s. d.	£ s. d.		£ s. d.	£ s. d.	£ s. d.		£ s. d.
	1500 0 0	To Sundry Creditors			8458 7 0	By Investments as per Schedule (cost or value when acquired)	3816 9 5
9086 0 7		„ Reserve for Publications as per last Balance Sheet	85 0 7		444 18 1	„ Cash at Bank and on Deposit in London Trustee Savings Bank	815 5 3
9000 0 0		*Deduct* Amount transferred to Publications Account...	— — —				
	85 0 7			85 0 7			
	1309 17 8	„ Reserve for Library Books and Binding as per last Balance Sheet		1300 17 8			
3350 0 0		„ Reserve for Research Fund as per last Balance Sheet	3350 0 0				
— — —		*Deduct* Amount transferred to Research Fund	3350 0 0				
	3350 0 0			— — —			
	825 0 0	„ Reserve for Building Fund		825 0 0			
1650 1 11		„ Excess of Income over Expenditure brought forward	2133 6 10				
51 19 6		*Add* Profit on transfer of Investments ...	15 0 0				
421 5 5		*Add* Excess of Income over Expenditure for year	286 12 2				
2123 6 10			2434 19 0				
— — —		*Deduct* Loss on transfer of Investments ...	23 2 7				
	2123 6 10			2411 16 5			
	£8903 5 1			£4631 14 8	£8903 5 1		£4631 14 8

THE CHEMICAL SOCIETY. BALANCE SHEETS, 31ST DECEMBER, 1950.

RESEARCH FUND.

1949 £ s. d.	£ s. d.	*Liabilities.*	£ s. d.	£ s. d.	1950 £ s. d.
	743 0 9	To Sundry Creditors		685 1 0	
20,689 8 10		„ Excess of Assets over Liabilities as per last Balance Sheet	20,877 15 10		
— — —		*Add* Amount received from Trustees of W. S. Gilles—Balance of Legacy ...	80 7 4		
— — —		*Add* Value of Investments transferred from Special Reserve Fund	3350 0 0		
20,689 8 10			24,008 3 2		
111 13 0		*Deduct* Excess of Expenditure over Income for year	79 14 2		
	20,577 16 10			23,928 9 0	
	£21,320 16 7			£24,613 10 0	

1949 £ s. d.	£ s. d.	*Assets.*	£ s. d.	£ s. d.	1950 £ s. d.
		By Sundry Debtors		27 0 0	
19,492 17 3		„ Investments as per Schedule (cost or value when acquired)		23,923 4 7	
1,827 19 4		„ Cash at Bank and on deposit in Post Office Savings Bank		663 5 5	
	£21,320 16 7			£24,613 10 0	

SPECIAL PUBLICATIONS FUND.

£ s. d.	£ s. d.	*Liabilities.*	£ s. d.	£ s. d.	£ s. d.
	65 7 3	To Sundry Creditors		32 15 10	
— — —		„ Cumulative Index to the Annual Reports, 1904–1949 (prepaid)		387 18 7	
3307 5 11		„ Excess of Assets over Liabilities as per last Balance Sheet	2825 4 8		
— — —		*Add* Excess of Income over Expenditure for year	123 11 7		
3307 5 11			2948 16 3		
382 1 3		*Deduct* Excess of Expenditure over Income for year	— — —		
	2923 4 8			2948 16 3	
	£3390 11 11			£3369 8 8	

1949 £ s. d.	£ s. d.	*Assets.*	£ s. d.	£ s. d.	1950 £ s. d.
20 11 4		By Sundry Debtors		22 8 11	
— — —		„ Cumulative Index to the Annual Reports, 1904–1949 (Preliminary Expenses)		107 7 11	
2011 19 10		„ Investments as per Schedule (cost or value when acquired)		2011 19 10	
858 0 9		„ Cash at Bank and on deposit in the Post Office Savings Bank and London Trustee Savings Bank		1226 13 0	
	£3390 11 11			£3369 8 8	

STAFF PENSIONS FUND.

£ s. d.	£ s. d.	*Liabilities.*	£ s. d.	£ s. d.	£ s. d.
	6 14 3	To Sundry Creditors		130 11 6	
5088 15 1		„ Excess of Assets over Liabilities as per last Balance Sheet	4681 15 9		
160 8 6		*Add* Profit on sale of Investments	— — —		
5249 3 7			4681 15 9		
537 7 10		*Deduct* Excess of Expenditure over Income for year	559 2 0		
	4681 15 9			4122 13 9	
	£4688 10 0			£4253 5 3	

£ s. d.	£ s. d.	*Assets.*	£ s. d.	£ s. d.	£ s. d.
300 0 0		By Sundry Debtors		— — —	
3726 6 0		„ Investments as per Schedule (cost or value when acquired)		3726 6 0	
663 4 0		„ Cash at Bank and on deposit in the Post Office Savings Bank		526 19 3	
	£4688 10 0			£4253 5 3	

THE CHEMICAL SOCIETY. BALANCE SHEETS, 31ST DECEMBER, 1950.

THE EDWARD FRANK HARRISON MEMORIAL TRUST FUND.

1949 £ s. d.		£ s. d.	1950 £ s. d.		1949 £ s. d.		1950 £ s. d.
	Liabilities.			*Assets.*			
	2 6 10	To Sundry Creditors	2 16 11		1101 7 11	By Investments as per Schedule (cost or value when acquired)	1101 7 11
1146 19 9		„ Excess of Assets over Liabilities as per last Balance Sheet	1191 9 9		92 6 8	„ Cash at Bank	119 14 8
44 10 0		*Add* Excess of Income over Expenditure for year	26 15 11				
	1191 9 9		1218 5 8				
	£1193 16 7		£1221 2 7		£1193 16 7		£1221 2 7

SPECIAL LECTURES FUND.

£ s. d.	£ s. d.		£ s. d.	£ s. d.	£ s. d.		£ s. d.
	1 14 4	To Sundry Creditors	2 17 4		1515 5 0	By Investment as per Schedule (cost or value when acquired)	1615 5 0
1582 0 11		„ Excess of Assets over Liabilities as per last Balance Sheet	1614 13 8		101 3 0	„ Cash at Bank	31 16 8
32 12 9		*Add* Excess of Income over Expenditure for year	29 10 5				
	1614 13 8		1644 4 1				
	£1616 8 0		£1647 1 5		£1616 8 0		£1647 1 5

THE FARADAY LECTURE FUND.

£ s. d.	£ s. d.		£ s. d.	£ s. d.	£ s. d.		£ s. d.
	13 9	To Sundry Creditors	18 11		439 4 0	By Investment as per Schedule (cost or value when acquired)	439 4 0
470 13 9		„ Excess of Assets over Liabilities as per last Balance Sheet	483 17 0		45 6 9	„ Cash at Bank	34 11 9
12 3 8		*Add* Excess of Income over Expenditure for year	— — —				
483 17 0			483 17 0				
— — —		*Deduct* Excess of Expenditure over Income for year	11 0 2				
	483 17 0		472 16 10				
	£484 10 9		£473 15 9		£484 10 9		£473 15 9

THE TILDEN LECTURE FUND.

1949			*Liabilities.*			1950		
£	s.	d.		£	s.	d.	£	s.	d.
			To Sundry Creditors				4	7	2
2014	2	3	„ Excess of Assets over Liabilities as per last Balance Sheet	1982	11	1			
			Add Excess of Income over Expenditure for year	15	16	3			
2014	2	3		1998	7	4			
31	11	2	*Deduct* Excess of Expenditure over Income for year						
		1982	11	1			1998	7	4
		£3010	19	11			£2002	14	6

1949			*Assets.*	1950		
£	s.	d.		£	s.	d.
1878	14	10	By Sundry Debtors	14	16	1
132	5	1	„ Investments as per Schedule (cost or value when acquired)	1878	14	10
			„ Cash at Bank (including Deposit)	109	1	7
£3010	19	11		£2002	14	6

CENTENARY FUND.

£	s.	d.		£	s.	d.	£	s.	d.	£	s.	d.
			To Sundry Creditors				235	6	2			
			„ Capital Account:									
14,624	9	4	Contributions under Deeds and Donations brought forward	17,332	6	8						
2,707	17	4	*Add* Contributions under Deeds and Donations for year	2,999	7	10						
		17,332	6	8			20,331	14	6			
			„ Excess of Income over Expenditure for year	202	15	11						
87	9	2	*Add* Excess of Income over Expenditure brought forward	120	11	3						
33	2	1					323	7	2			
		120	11	3								
		£17,530	13	9			£20,890	7	10	£20,890	7	10

£	s.	d.		£	s.	d.
			By Sundry Debtors	596	3	7
17,193	3	4	„ Investments as per Schedule (cost or value when acquired)	18,898	2	4
333	10	5	„ Cash at Bank	1,396	0	11
£17,530	13	9		£20,890	7	10

THE ROBERT JOHN FLINTOFF TRUST.

£	s.	d.		£	s.	d.	£	s.	d.	£	s.	d.
			To Sundry Creditors				1	6	6			
1000	0	0	„ Cash received from Executors									
			„ Excess of Assets over Liabilities as per last Balance Sheet	1003	17	2						
3	17	2	*Add* Excess of Income over Expenditure for year	25	3	5						
							1029	0	7			
£1003	17	2					£1030	7	1	£1030	7	1

£	s.	d.		£	s.	d.
			By Sundry Debtors	7	16	0
1000	0	0	„ Investments as per Schedule (cost or value when acquired)	1000	0	0
3	17	2	„ Cash at Bank	22	11	1
£1003	17	2		£1030	7	1

THE CHEMICAL SOCIETY. BALANCE SHEETS, 31ST DECEMBER, 1950.

THE CORDAY-MORGAN MEMORIAL FUND.

1949	*Liabilities.*	£ s. d.	1950 £ s. d.	1949	*Assets.*	1950
£ s. d.				£ s. d.		£ s. d.
	To Sundry Creditors		34 1 1		By Sundry Debtors	55 6 6
	„ Amount received from Public Trustee :—				„ Investments as per Schedule (cost or value when acquired)	8513 17 6
	On Capital Account		8513 17 6		„ Cash at Bank (including Deposit)	2183 2 0
	On Income Account (1944–1949)	1047 13 9				
	„ Income Tax recovered	1096 0 11				
		2142 14 8				
	Add Excess of Income over Expenditure for year ...	61 12 9				
			2204 7 5			
			£10,752 6 0			£10,752 6 0

THE CORDAY-MORGAN MEDAL AND PRIZE FUND.

£ s. d.		£ s. d.	£ s. d.	£ s. d.		£ s. d.
	To Sundry Creditors		5 0 3		By Sundry Debtors	28 10 6
	„ Amount received from Public Trustee :—				„ Investments as per Schedule (cost or value when acquired)	5785 17 9
	On Capital Account		4985 17 9		„ Cash at Bank (including Deposit)...	276 0 4
	On Income Account (1944–1949)	598 13 9				
	„ Income Tax recovered	631 10 9				
		1230 4 6				
	Less Cost of Design of Medal	188 8 0				
		1041 16 6				
	Add Excess of Income over Expenditure for Year... ...	67 14 1				
			1109 10 7			
			£6100 8 7			£6100 8 7

SCHEDULE OF INVESTMENTS.

GENERAL PURPOSES.

Nominal Details.	*Cost or Value when Acquired.*	*Market Value 31st December, 1950.*
	£ s. d.	£ s. d.
£2436 18s. 0d. 3½% Conversion Loan, 1961, or after	1884 12 8	2335 14 10
£2408 2s. 6d. 3% Funding Loan, 1959/69	2429 11 5	2384 0 10
£2400 14s. 9d. 3% Savings Bonds, 1960/70	2418 11 0	2370 14 7
£2000 3% Savings Bonds, 1965/75	2006 4 5	1935 0 0
£4747 4s. 5d. 3% British Transport Guaranteed Stock, 1978/88 ...	5704 9 8	4343 14 3
£3546 1s. 4d. 3% British Electricity Guaranteed Stock, 1968/73 ...	3549 4 5	2469 13 8
£1300 2½% Defence Bonds	1300 0 0	1300 0 0
£2400 2½% Bristol Corporation Debenture Stock, 1957	2070 2 0	2352 0 0
£1550 3½% London County Consolidated Stock, 1954/59	1639 2 6	1573 5 0
£2000 3% London County Consolidated Stock, 1962/67	2032 10 0	1970 0 0
£2500 3% Commonwealth of Australia Registered Stock, 1964/66 ...	2509 7 6	2462 10 0
£A3000 4% Commonwealth of Australia Treasury Bonds, 1961 ...	2552 16 7	2430 0 0
	£38,996 12 2	£37,826 13 2

PUBLICATIONS FUND.

£2260 19s. 9d. 3½% Conversion Loan, 1961, or after	1566 16 4	2176 2 11
£1000 3% Savings Bonds, 1955/65	1000 0 0	1012 10 0
£2261 1s. 11d. 3% Savings Bonds, 1960/70	2276 1 11	2232 16 8
£2175 12s. 4d. 3% British Transport Guaranteed Stock, 1978/88 ...	1929 1 4	1990 14 9
£2000 3% British Electricity Guaranteed Stock, 1968/73	2002 10 0	1940 0 0
£1200 3% Commonwealth of Australia Registered Stock, 1964/66 ...	1204 10 0	1163 0 0
£963 12s. 0d. 3% Southern Rhodesia Stock, 1971/73	1000 0 0	983 2 8
	£10,978 19 7	£11,487 7 9

SPECIAL RESERVE FUND.

£1165 3½% Funding Loan, 1956/61	1169 7 8	1162 1 9
£2582 10s. 9d. 3% Liverpool Corporation Stock, 1955/58	2647 2 0	2608 7 3
	£3816 9 8	£3770 9 0

CORDAY-MORGAN MEMORIAL FUND.

Nominal Details.	*Cost or Value when Acquired.*	*Market Value 31st December, 1950.*
	£ s. d.	£ s. d.
£343 15s. 0d. 3½% Conversion Loan, 1961, or after	320 0 0	330 17 3
£1973 16s. 11d. 3½% War Stock, 1952, or after	1880 1 10	1860 7 0
£477 1s. 10d. 3% British Electricity Guaranteed Stock, 1968/73 ...	450 17 0	461 11 9
£273 15s. 4d. 3% British Gas Guaranteed Stock, 1990/95	247 15 2	249 16 3
£217 12s. 6d. 3% London County Consolidated Stock, 1962/67 ...	208 7 6	214 7 3
£300 4½% Hull Corporation Stock, 1952/72	303 15 0	307 10 0
£412 10s. 0d. 3% City of Plymouth Stock, 1954	405 5 7	425 18 2
£157 10s. 0d. 4½% Kenya Government Stock, 1961/71	148 16 11	151 18 9
£300 3% New Zealand Government Stock, 1952/53	298 10 0	304 10 0
£68 Barclays Bank, Ltd., "B" Ordinary £1 Stock Units	237 3 0	238 6 0
£206 Benskins Watford Brewery, Ltd., Ordinary £1 Shares	684 19 0	688 17 3
£206 H. & G. Simmonds, Ltd., Ordinary £1 Stock Units	524 0 0	732 15 5
£100 Imperial Tobacco (G.B. & I.) Ltd., Ordinary £1 Shares	506 5 0	512 10 0
£108 Thomas Tilling & Co., Ltd., Ordinary £1 Stock Units	107 4 6	126 18 0
£340 Alliance Trust, Ltd., 4½% Debenture Stock, 1956	344 5 0	350 4 0
£69 London & Lancashire Insurance Co., Ltd., Ordinary £1 Stock Units	448 10 0	474 7 6
£68 Phœnix Assurance Co., Ltd., Ordinary £1 Stock Units	1088 0 0	1902 15 0
	£8513 17 6	£8652 9 6

CORDAY-MORGAN MEDAL AND PRIZE FUND.

£1398 5s. 4d. 3½% War Stock, 1952, or after	1335 14 0	1317 17 4
£206 5s. 0d. 4% Consolidated Stock, 1957, or after	213 9 4	211 8 3
£137 10s. 0d. 3½% Bournemouth Corporation Stock Red., 1958/63 ...	133 14 5	138 17 4
£206 5s. 0d. 4½% Bristol Corporation Stock, 1952/62	208 16 7	213 9 4
£206 5s. 0d. 4½% Hertfordshire County Council Stock, 1958/68 ...	216 0 4	220 13 9
£300 3½% Hertfordshire County Council Stock, 1954/59	297 15 0	312 0 0
£206 5s. 0d. 3% British Guiana Government Stock, 1979/80	190 5 4	194 0 1
£137 10s. 0d. 3% Federated Malay States Government Stock, 1960/70	130 6 5	127 3 9
£90 Barclays Bank (D. C. & O.) Ltd., "A" Ordinary £1 Stock Units	201 7 6	204 15 0
£172 Mitchells & Butlers, Ltd., Ordinary £1 Stock Units	713 16 0	600 10 5
£206 Watney, Coombe & Reid, Ltd., Deferred Ordinary £1 Shares ...	307 5 0	330 9 0
£52 Imperial Tobacco Co. (G.B. & I.) Ltd., Ordinary £1 Shares ...	263 5 0	266 10 0
£240 Cardinal Investment Trust, Ltd., 3½% Debenture Stock	291 0 0	283 4 0
£104 Commercial Union Assurance Co., Ltd., Ordinary £1 Stock Units	1014 0 0	1144 0 0
	£5785 17 9	£5864 18 4

SCHEDULE OF INVESTMENTS.

CENTENARY FUND.

Nominal Details.	Cost or Value when Acquired.	Market Value 31st December, 1950.
	£ s. d.	£ s. d.
£2477 13s. 11d. 3% Savings Bonds, 1955/65	2491 11 10	2508 15 4
£2500 3% Savings Bonds, 1960/70	2534 7 6	2468 15 0
£2705 18s. 7d. 2½% Savings Bonds, 1964/67	2500 0 0	2557 2 1
£2979 13s. 0d. 3% British Transport Guaranteed Stock, 1978/88 ...	2237 7 9	2085 17 7
£2500 3% British Electricity Guaranteed Stock, 1968/73	2498 8 9	2425 0 0
£1970 1s. 0d. 3% New Zealand Stock, 1973/77	2000 0 0	1881 7 11
£1716 15s. 2d. 3½% Northern Ireland Stock, 1969/71	1700 0 0	1700 0 0
£A3500 4% Commonwealth of Australia Treasury Bonds, 1961 ...	2936 7 6	2940 0 0
	£18,896 3 4	£18,566 15 11

THE FARADAY LECTURE FUND.

£441 1s. 11d. 3½% Conversion Loan, 1961, or after	£439 4 0	£424 11 1

ROBERT JOHN FLINTOFF TRUST.

£522 2s. 2d. 3½% Conversion Loan, 1961, or after	500 0 0	503 9 10
£545 19s. 4d. 3% British Transport Guaranteed Stock, 1978/88 ...	500 0 0	499 11 2
	£1000 0 0	£1003 1 0

RESEARCH FUND.

£4177 16s. 1d. 3½% Conversion Loan, 1961, or after	3625 16 8	4021 2 9
£500 Defence Bonds, 4th issue	500 0 0	500 0 0
£1835 2½% Funding Loan, 1956/61	1835 0 0	1830 8 3
£1500 3% Savings Bonds, 1955/65	1518 0 0	1518 15 0
£4000 3% Savings Bonds, 1960/70	4060 0 0	3950 0 0
£3755 2s. 1d. 3% British Transport Guaranteed Stock, 1978/88 ...	3567 19 5	3435 18 5
£3719 8s. 2d. 3% British Electricity Guaranteed Stock, 1968/73 ...	3724 1 2	3607 16 6
£4000 3% Commonwealth of Australia Registered Stock, 1964/66 ...	4015 0 0	3940 0 0
£1116 7s. 0d. 3% New Zealand Stock, 1973/77	1080 7 4	1066 2 4
	£23,923 4 7	£23,870 3 3

THE EDWARD FRANK HARRISON MEMORIAL TRUST FUND.

Nominal Details.	Cost or Value when Acquired.	Market Value 31st December, 1950.
	£ s. d.	£ s. d.
£61 15s. 8d. 2½% Conversion Loan, 1961, or after	50 1 5	59 9 4
£1489 10s. 6d. 3% British Transport Guaranteed Stock, 1978/88 ...	1051 6 6	1362 18 4
	£1101 7 11	£1422 7 8

SPECIAL LECTURES FUND.

£1669 17s. 5d. 3% British Transport Guaranteed Stock, 1978/88 ...	£1615 5 0	£1527 18 6

SPECIAL PUBLICATIONS FUND.

£715 8s. 10d. 3½% Conversion Loan, 1961, or after	541 2 4	688 12 3
£746 1s. 0d. 3% British Transport Guaranteed Stock, 1978/88 ...	719 18 9	682 12 9
£750 3% British Electricity Guaranteed Stock, 1968/73	750 18 9	727 10 0
	£2011 19 10	£2098 15 0

STAFF PENSIONS FUND.

£114 1s. 11d. 3½% Conversion Loan, 1961, or after	88 2 3	109 16 4
£150 2½% National War Bonds, 1951/53	150 0 0	151 2 6
£170 3% Savings Bonds, 1955/65	170 0 0	167 17 6
£815 2s. 7d. 2½% Funding Loan, 1956/61	818 3 9	811 1 1
£3800 2½% Defence Bonds	2800 0 0	2800 0 0
	£3726 6 0	£3739 17 5

THE TILDEN LECTURE FUND.

£419 4s. 10d. 3% Funding Loan, 1959/69	386 12 10	415 0 11
£681 19s. 1d. 3% British Transport Guaranteed Stock, 1978/88 ...	625 2 0	623 19 9
186 National Provincial Bank Shares £5 each, £1 paid "B"	678 18 0	664 19 0
£220 3% Metropolitan Water Board (Kent Water Works) Deb. Stock	188 2 0	184 16 0
	£1878 14 10	£1888 15 8

W. A. AKERS, *Treasurer.*

We have examined the above Balance Sheets and accompanying Income and Expenditure Accounts with the Books and Vouchers of the Society, and certify them to be in accordance therewith and, in our opinion, correct. We have also verified the Balances at the Bankers and Investments.

FINSBURY CIRCUS HOUSE,
BLOMFIELD STREET, E.C.2.
MARCH 15TH, 1951.

W. B. KEEN & CO.
Chartered Accountants.

SYMBOLS, SIGNS, AND ABBREVIATIONS

RECOMMENDED FOR BRITISH SCIENTIFIC PUBLICATIONS

A REPORT

BY

THE SYMBOLS COMMITTEE OF THE ROYAL SOCIETY

REPRESENTING

THE ROYAL SOCIETY
THE CHEMICAL SOCIETY
THE FARADAY SOCIETY
THE PHYSICAL SOCIETY

1951

Superseding the Report of the Joint Committee of the Chemical Society, the Faraday Society and the Physical Society on 'Symbols for Thermodynamical and Physico-Chemical Quantities and Conventions relating to their Use', issued in 1937

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INTRODUCTION

In 1937 a joint committee of the Chemical Society, the Faraday Society, and the Physical Society issued a *Report on Symbols for Thermodynamical and Physico-Chemical Quantities and Conventions relating to their Use* (CFP, 1937). A few minor amendments were made at the instance of the Royal Society, and the *Report* was then adopted as the basis of practice in the publications of the four Societies and of a number of other British bodies, including the Bureau of Abstracts. The recommendations in the *Report* were given further publicity in the following year when they were embodied (with additional recommendations on abbreviations) by the British Standards Institution in British Standard *Chemical Symbols and Abbreviations* (B.S. 813—1938).

In the preparation of CFP, 1937, attention was given to usages adopted by authors of well-known text-books, as well as to recommendations in earlier reports of other bodies dealing with symbols, including the International Conference on Physics, 1934, the Informal International Conference on Letter Symbols for Heat and Thermodynamics, 1936, and, as regards electrical quantities, the International Electrotechnical Commission. In submitting the *Report*, the joint committee drew special attention to the fact that, although recommendations on the use of physico-chemical symbols had been put forward in the past by a number of bodies, these bodies had nearly always been representative of either physicists or chemists, and not, as in that instance, of both. It was recognized that this constituted an important advance, for by bringing physicists and chemists together many differences had been readily adjusted and a wide measure of agreement attained over the whole of their combined fields of interest.

In order that the advantages of this co-operation should not be lost, the Royal Society set up in 1938 a standing committee on Symbols (R.S. Symbols Committee), on which the Chemical Society, the Faraday Society, and the Physical Society are represented, to consider from time to time any directions in which CFP, 1937, should be revised. In accordance with this undertaking the Royal Society Symbols Committee has drafted the present Report (RCFP, 1951) which has since been adopted by the four Societies concerned as superseding CFP, 1937, and is now put forward as recommended practice in British scientific publications.

Since the war the correlation of the views of physicists and chemists on the use of symbols has been carried further at international level. At the Conference of the International Union of Chemistry in London in 1947, its Commission on Physico-Chemical Symbols and Co-ordination of Scientific Terminologies (P.C.S. Commission) accepted most of the general principles enunciated in CFP, 1937, and adopted, at least as acceptable alternatives, a majority of the symbols recommended for individual quantities; the conclusions of the Commission were published in the *Report* of the Conference (IUC, 1947). At its meetings in London the Commission had the benefit of the advice of representatives of the Symbols, Units, and Nomenclature Commission (S.U.N. Commission) of the International Union of Pure and Applied Physics, who were present by invitation. At the Conference of the latter Union in Amsterdam in 1948, the S.U.N. Commission took cognizance of relevant recommendations in recent reports of national and international bodies, including IUC, 1947. Its own *Report* (IUPAP, 1948) covered much common ground, but naturally extended further into the field of pure and applied physics. In the following year a Conference of the International Union of Pure and Applied Chemistry (which had then reverted to this earlier title) was held in Amsterdam, when its P.C.S. Commission revised IUC, 1947, with special regard to securing the widest measure of agreement with IUPAP, 1948. In the resulting *Report* (IUPAP, 1949) the recommendations in IUC, 1947, and IUPAP, 1948, were almost completely reconciled and co-ordinated, and recommendations in the latter referring to symbols for quantities mainly of interest to physicists were incorporated so as to provide in one *Report* the agreed conclusions of chemists and physicists.

In preparing the present *Report* (RCFP, 1951) the R.S. Symbols Committee has given special attention to the recommendations of these International Commissions and has not departed from them, except, in certain instances, by selecting from alternative symbols for a quantity

the one which is most in accord with British usage and, in a few cases, by introducing other alternatives to avoid clashes with symbols for different quantities that may appear in the same equations. Such deviations from the international recommendations have thus been essentially in points of detail and have not arisen from any disagreement on matters of general principle.

In the course of its work, the R.S. Symbols Committee has also maintained close touch with the British Standards Institution, whose Technical Sub-Committee, OC/22/1, has been concurrently engaged in the revision and co-ordination of the existing British Standards *Engineering Symbols and Abbreviations* (B.S. 560—1934) and *Chemical Symbols and Abbreviations* (B.S. 813—1938). In so far as this leads to widening the scope of agreement between physicists and chemists to meet the needs of engineers—at least in respect of symbols for the more fundamental quantities of common interest—a further important step will have been taken towards removing differences of usage in the various branches of pure and applied science and thus providing a firm basis on which to develop consistent practice in more specialized fields.

RECOMMENDATIONS

I. GENERAL PRINCIPLES

(*a*) Alphabets and Founts

In order to make the best use of the limited number of readily available alphabets and founts, it is strongly recommended that the undermentioned principles, already generally approved at international level, should be adopted and strictly followed.

A clear distinction is to be drawn between :

(1) *Symbols for physical quantities* (*see* Schedule A, 1—10) :

These normally consist of single letters of the Latin or the Greek alphabet (sometimes with subscripts or other modifying signs—*see* Schedule B) which are used to represent the quantities concerned, especially in equations showing relationships between them. For a particular quantity the same symbol is to be used irrespective of the units in which it is expressed.

Where letters of the Latin alphabet (*capitals or lower case*) *are used for this purpose, they are to be printed in italic* (*sloping*) *type* except that for vector quantities the customary heavy-faced sans serif type may be used (*see* Schedule A, 9), and where so used for one such quantity must be employed consistently for others in the same discussion. A further permissive variation is the use of bold italic type for certain general constants (*see* Schedule A, 1); if this variation is adopted it should also be applied consistently.

(2) *Other symbols and abbreviations*, including :

(i) those denoting mathematical operations and constants (*see* Schedule C);
(ii) symbols for the chemical elements;
(iii) abbreviations for words (*see* Schedules D and E), including abbreviations (symbols) for the names of units (Schedule D).

Where letters of the Latin alphabet (*capitals or lower case*) *are used for any of these purposes, they are to be printed in* roman (*upright*) *type.*

It is not suggested that where Greek letters are involved any attempt should be made to use a sloping fount for symbols for physical quantities and an upright fount for other symbols and abbreviations, though this differentiation has been made for capital letters in the schedules to indicate the possibilities of this refinement. It is useful, however, to use bold Greek letters for certain specified general constants wherever the practice of printing letters of the Latin alphabet for these quantities in bold italic type is adopted (*see* Schedule A, 1).

By making the broad distinction between symbols for physical quantities—to be printed in a sloping fount of type—and other symbols and abbreviations—to be printed in an upright fount of type—at least in so far as letters of the Latin alphabet (including capital letters) are concerned, the pressure on certain overworked letters is notably relieved. A further relief is secured if bold type (italic or Greek) is employed for symbols for general constants; this has the additional advantage of causing these symbols to stand out against those for variables in equations. Thus, e can be used to denote the base of natural logarithms (a purely mathematical constant—Schedule C), and $\boldsymbol{e}$ to represent the magnitude of the charge of the electron (a physical constant—Schedule A, 1), leaving e for physical variables. Similarly, the use of d to denote the operation of differentiation (Schedule C) leaves d available for physical quantities such as " diameter ", " relative density ", or " current density at an electrode ", but in this particular instance the alternative d is to be regarded as permissive. Again, demands on E for several physical quantities, of which more than one may occur in a single equation, can be partly relieved by adopting $\mathbf{E}$ for electric force or field strength.

Nevertheless, even with these provisions for the use of different founts, the number of distinctive letter symbols available for physical quantities is insufficient to enable each such symbol to be allotted to a single quantity, and alternatives are therefore required in some

instances. Such alternatives are given in the schedules where a need for them is most likely to arise or, in a few cases, where alternative usages are firmly established and unobjectionable. ***Where two or more symbols separated by commas are given for a quantity, these symbols are to be regarded as alternatives for which no preference is expressed; where they are separated by a dotted line, the former is the first preference.*** Where it is necessary to select from alternative symbols for a quantity, or to adopt a symbol for a quantity not listed, consideration should be given to current practice by authorities in the field and to the desirability that ***symbols for quantities constituting a well-defined class should, if possible, belong to the same alphabet, fount and case.*** The selected symbols should be such as to permit of modification in accordance with a uniform scheme for the representation of any important series of corresponding derived quantities.

Abbreviations for words, including abbreviations (symbols) for the names of units, may be used in the text of papers and, in so far as they represent words that vary from one language to another (*see* Schedule E), they are not susceptible to international agreement. Moreover, although it is desirable to secure as wide a measure of agreement as may be readily achieved in English-speaking countries on abbreviations for words in common scientific use, failure to achieve such agreement in respect of individual words should not be regarded as so serious a matter as any disagreement on symbols for physical quantities. It is more important, however, to get agreement on ***abbreviations*** (*or symbols*) ***representing the names of internationally accepted units*** (*see* Schedule D, 1). These may consist of single letters (such as V for volt), or of several letters (such as kWh for kilowatt-hour), and ***are used following*** (*or preceding*) ***a number*** (e.g., 1·236 V; pH 5·3) ***and never as symbols for the corresponding physical quantities in equations.*** A single-letter abbreviation for the name of a unit which is identical with or derived from a personal name should always be a capital letter (*see also* below).

(*b*) Other General Principles

Mathematical Usages. There should be no departure from the standard practice of mathematicians in the use of signs, operator symbols, etc. (*see* Schedule C). Numbers should be printed in upright figures. A decimal point should be used to separate whole numbers from the decimals. To facilitate the reading of large numbers the figures may be grouped together in threes, but no commas should be used to separate the groups.

Use of Modifying Signs. For the use of modifying signs such as subscripts, superscripts, and brackets (for examples *see* Schedule B) no rigid rules are laid down, but a satisfactory notation should fulfil the following requirements:

(i) It should be unambiguous.
(ii) It should be systematic, simple and easy to remember.
(iii) It should not be extravagant in using up more letters of the alphabet than necessary.
(iv) It should not be expensive or difficult to print.

The notation ln and log would be preferable to $\log_e$ and $\log_{10}$ respectively because of condition (iv), were it not for condition (i). The use of ln and $\log_{10}$ is encouraged for the time being in the hope that the use of ln may become universal, and it will then be safe to abbreviate $\log_{10}$ to log.

Brackets, including parentheses ( ), braces { }, and square brackets [ ] should not be used around the symbol for a quantity in order to make it represent any other quantity, unless such use is consistently adopted for a whole class of quantities as in crystallography. The use of brackets or braces around a chemical formula to denote, respectively, the molar concentration or the relative activity of the substance fulfils the above general and particular requirements. Most other uses of brackets, apart from their mathematical uses, do not fulfil these requirements.

Conventions for the Representation of Thermodynamic Data for Chemical Reactions. It is recommended that thermodynamic data for chemical reactions be expressed by quoting the equation for the reaction (with such specification of the physical states of participating substances as may be necessary) followed by the magnitude of the change (positive or negative) in the appropriate thermodynamic function. For example, for the heat of reaction at a constant pressure of 1 atm

$$CH_3{\cdot}OH\ (\text{liq.}) + 1\tfrac{1}{2}O_2 = CO_2 + 2H_2O\ (\text{liq.})$$
$$-\Delta H\ (\text{at } 298^\circ\text{ K}) = 726{\cdot}93\ \text{kJ}$$

Similarly, for the heat of the same reaction at constant volume

$$-\Delta U\ (\text{at } 298^\circ\text{ K}) = 728{\cdot}18\ \text{kJ}$$

It is preferred that quantities of heat, as of other forms of energy, be expressed in joules; where data are given in calories the corresponding values in joules should be added, with the conversion factor used. The use of a special symbol to denote the heat *evolved* in a chemical reaction—as was formerly customary in thermochemistry—is not recommended.

Conventions concerning Abbreviations. Abbreviations for the name of units are the same in the singular and the plural, *i.e.*, no 's' is to be added when the magnitude is greater than unity.

No definite rule is prescribed for the use of a full point after an abbreviation, but the recommendation is that such points are preferably omitted • wherever this can be done without causing ambiguity (l. is used for litre in order to avoid confusion with the numeral one), and should always be omitted after single capital letters representing the names of units (*see* Schedule D). It is customary however to use a full point after abbreviations for words used in the text and for the names of British units.

II. SPECIFIC USAGES

A. Symbols for Physical Quantities

(Letters of the Latin alphabet used for this purpose are to be printed in italic type, except in so far as a heavy-faced sans serif type may be employed for vector quantities.)

1. *General Constants.*

(Symbols for these constants may be printed in **bold** *type—italic or Greek—to distinguish them from variables. For purely mathematical constants, see Schedule C.)*

speed of light	$\boldsymbol{c}, c$	Planck's constant	$\boldsymbol{h}, h$
Avogadro's number	$\boldsymbol{N}, N$	Bohr's magneton	$\boldsymbol{\beta}, \beta$
gas constant per mole	$\boldsymbol{R}, R$	Rydberg's constant	$\boldsymbol{R}, R$
Boltzmann's constant	$\boldsymbol{k}, k$	Stefan–Boltzmann constant	$\boldsymbol{\sigma}, \sigma$
Faraday's constant	$\boldsymbol{F}, F$	gravitational constant	$\boldsymbol{G}, G$
charge of electron	$-\boldsymbol{e}, -e$	gravitational acceleration,	
mass of electron	$\boldsymbol{m}, m$	standard value	$\boldsymbol{g}, g_0$

2. *Mensuration.*

length	l	rectangular coordinates	x, y, z
height	h	cylindrical coordinates	$r, \phi, z \ldots \rho, \phi, z$
breadth	b	spherical coordinates	r, θ, ϕ
radius	r		
diameter	d	angle, plane	α, β; θ, ϕ, etc.
		angle, solid	ω
area	A		
volume	V, v		

3. *Kinematics.*

time	t	velocity	v, u
period	T	velocity, angular	ω
frequency	f, ν	acceleration	$a \ldots f$
wave number	$\nu, \tilde{\nu}$	acceleration, angular	α
wave-length	λ	acceleration, gravitational	g

• Nevertheless, full points will be used in the Chemical Society's publications after abbreviations in lower-case letters for all units.

4. *Mechanics.*

mass	m	Young's modulus	E
density	ρ	rigidity	G
density, relative	d	bulk modulus	K
		compressibility	κ
force	F	Poisson's ratio	$\sigma \dots \nu$
weight	W		
moment	M		
pressure	p, P	bending moment	M
		torque	T
work	W, w	modulus of section	Z
energy	E, W		
energy, kinetic	T	coefficient of friction	μ
energy, potential	V	viscosity	η
power (*see also section* 9)	P	fluidity	ϕ
efficiency	η	viscosity, kinematic	ν
moment of inertia	I	surface tension	γ, σ
radius of gyration	k		

5. *Thermodynamics.*

temperature, empirical	$\theta \dots t$	internal energy	U
temperature, absolute	T	entropy	S
thermal conductivity	λ, k	free energy (Helmholtz function)	F
		heat function; enthalpy; total heat	H
quantity of heat	Q, q	Gibbs function	G
thermal expansion, coefficient of	α		
		partition function	Q
heat capacity per unit mass	c		
heat capacity per mole	C		
ratio of specific heats	γ		
Joule–Thomson coefficient	μ		

6. *Chemical Composition and Reaction.*

atomic number	Z	concentration	c, C
atomic weight	A	concentration, molar, of substance X	$c_X, C_X, [X]$
molecular weight	M	molality	m
number of molecules	N	surface concentration	Γ
number of moles	n		
stoichiometric number of molecules	ν	diffusion coefficient	D
degree of dissociation (*see also section* 10)	α		
		velocity constant (of reaction)	k
mole fraction	x	activation energy (of reaction)	E
weight fraction	w	equilibrium constant (of reaction)	K
volume fraction	ϕ		

7. *Chemical Thermodynamics.*

chemical potential	μ	activity coefficient (*see also section* 10)	f, γ
activity, absolute	λ		
activity, relative	a	osmotic pressure	Π
activity, relative, of substance X	a_X, {X}	osmotic coefficient	g

8. *Light.*

luminous flux	F, Φ
luminous intensity	I
luminance; brightness (photometric)	L, B
luminance factor	β
luminous radiance	R
illumination	E
absorption factor	a
reflexion factor	ρ
transmission factor	τ
refractive index	$n \ldots \mu$ (with subscript)

9. *Electricity and Magnetism.*

electromotive force (*see also section* 10)	E, V
potential; potential difference	V
electric current	I
electric charge	Q
resistance	R
inductance	L
capacitance	C
electric force; electric field strength	$\mathbf{E}, E$
electric flux density; electric displacement	$\mathbf{D}, D$
magnetic flux density; magnetic induction	$\mathbf{B}, B$
magnetic field strength; magnetizing force	$\mathbf{H}, H$
permittivity	ϵ
permittivity, relative; dielectric constant	ϵ_r, ϵ
permittivity, of free space	ϵ_0
permeability	μ
permeability, relative	μ_r, μ
permeability, of free space	μ_0
magnetic vector potential	$\mathbf{A}, A$
electric flux	Ψ
magnetic flux	Φ
current density (*see also section* 10)	$\mathbf{J}, J$
intensity of magnetization; magnetic polarization	$\mathbf{M}, M \ldots \mathbf{I}, I$
Poynting vector	$\mathbf{S}, S$
magnetic susceptibility (volume)	κ
magnetic susceptibility (mass)	χ
charge density (volume)	ρ
charge density (surface)	σ
electronic exit work function	ϕ
resistivity; specific resistance	ρ, r
conductivity; specific conductance (*see also section* 10)	σ, γ
dipole moment, electric or magnetic	μ
resistance	R
reactance	X
impedance	Z
conductance	G
susceptance	B
admittance	Y
inductance, self	L
inductance, mutual	M
inductance, self or mutual	L (with subscripts)
energy, electrical	W
power (*see also section* 4)	P
power, reactive	Q
power, apparent (or ' volt-amperes ')	S
phase difference	ϕ
power factor	$\cos \phi$
dielectric loss angle	δ

10. *Electrochemistry.*

degree of electrolytic dissociation (*see also section* 6)	α
valency of an ion	z (negative for anion)
ionic strength	I
activity coefficient (*see also section* 7)	f
activity coefficient, stoichiometric (*see also section* 7)	γ
conductivity; specific conductance (*see also section* 9)	κ
conductance, equivalent or (with subscript m) molar	Λ
ionic conductance, equivalent	$\Lambda \ldots l$ (with subscript)
transport number	t, T (with subscript)
electromotive force of voltaic cell (*see also section* 9)	E
single electrode potential	E (with subscript)
current density at an electrode surface (*see also section* 9)	d
electrolytic polarization; overpotential	η
electrokinetic potential	ζ

B. Examples of Subscripts and Other Modifying Signs

1. *Subscripts to Symbols for Quantities.*

I, II ... 1, 2 ...	*especially with symbols for thermodynamic functions*, referring to different systems or different states of a system.
A, B ...	referring to molecular species A, B, etc.
i	referring to a typical ionic species *i*.
u	referring to an undissociated molecule.
+, −	referring to a positive or negative ion, or to a positive or negative electrode.
p, *v*, *T*, *S*	indicating constant pressure, volume, temperature, and entropy respectively.
p, *c*, *a*	*with symbol for an equilibrium constant*, indicating that it is expressed in terms of pressure, concentration, or activity.
g, l, s, x	referring to gas, liquid, solid and crystalline states respectively.
f, *e*, *s*, *t*, *d*	referring to fusion, evaporation, sublimation, transition, and dissolution or dilution respectively.
c	referring to the critical state or indicating a critical value.
0	indicating limiting value at infinite dilution.
C, D, F	*with symbols for optical properties*, referring to particular wave-lengths.

Where a subscript has to be added to a symbol which already carries a subscript, the two subscripts should be separated by a comma.

Some of the above subscripts may sometimes be more conveniently used as superscripts.

2. *Other Modifying Signs.*

[ ]	*enclosing formula of chemical substance*, indicating its molar concentration.
{ }	*enclosing formula of chemical substance*, indicating its relative activity.

In crystallography it is recommended that:

Millerian indices be enclosed in parentheses, ( );
Laue indices be unenclosed;
indices of a plane family be enclosed in braces, { };
indices of a zone axis or line be enclosed in square brackets, [ ].

Numerals attached to a symbol for a chemical element in various positions have the following meanings:

upper left	mass number of atom,
lower left	nuclear charge of atom,
lower right	number of atoms in molecule;

e.g., ${}^{7}_{3}\mathrm{Li}$; ${}^{2}_{1}\mathrm{H}_{2}$.

Ionic charge should be indicated by a superscript plus or minus sign following the symbol of the ion; for multiple charges an Arabic superscript numeral should precede the plus or minus sign; *e.g.*, Na^{+}, NO_3^{-}, Ca^{2+}, PO_4^{3-}, ${}^{7}_{3}\mathrm{Li}^{-}$.

A valency state should be indicated by a superscript Roman numeral following the symbol of the element; *e.g.*, $\mathrm{Sn}^{\mathrm{II}}$, $\mathrm{Sn}^{\mathrm{IV}}$.

In the formula of a free radical the unshared valency should be indicated by a bold-type point in the middle position; *e.g.*, $\mathrm{H_3C}^{\bullet}$, $\mathrm{C_6H_5}^{\bullet}$, $\mathrm{HO}^{\bullet}$.

C. Examples of Symbols and Abbreviations Denoting Mathematical Operations and Constants

(Letters of the Latin alphabet used for this purpose are to be printed in roman type.)

limit of y	$\lim y$
tends to a	$\to a$
average of several values of x	$\bar{x}$
sum of	Σ
product of	Π
division by (solidus), *e.g.*, g/cm²s	$/$
square root	$\sqrt{}$
nth root	$\sqrt[n]{}$
base of natural logarithms	e ... ε
logarithm of x to base e	$\ln x$ ... $\log_e x$
logarithm of x to base 10	$\log_{10} x$
antilogarithm	antilog
exponential function of x	$\exp x$, e^x
factorial n	$n!$
ratio of circumference to diameter of circle	π
trigonometric functions of θ	$\sin\theta$, $\cos\theta$, $\tan\theta$, $\operatorname{cosec}\theta$, $\sec\theta$, $\cot\theta$
inverse trigonometric functions	$\sin^{-1}\theta$ ... arc sin θ, etc.
hyperbolic functions of x	sihh x, $\cosh x$, $\tanh x$, $\operatorname{cosech} x$, $\operatorname{sech} x$, $\coth x$
inverse hyperbolic functions	$\sinh^{-1} x$, etc.
increment or finite difference operator	Δ, δ
•differential coefficient of y with respect to x	$\frac{dy}{dx}$, dy/dx
•differential coefficient, nth	$\frac{d^n y}{dx^n}$, $d^n y/dx^n$
differential coefficient, partial	$\frac{\partial y}{\partial x}$, $\partial y/\partial x$
operator $\frac{\partial}{\partial x}$ or with single variable $\frac{d}{dx}$	D
•integral of y with respect to x	$\int y\,dx$
•integral of y from $x = a$ to $x = b$	$\int_a^b y\,dx$
•integral of y around a closed contour	$\oint y\,dx$
complex operator $\sqrt{(-1)}$	i, j
real part of	$\mathscr{R}$
imaginary part of	$\mathscr{I}$
modulus of complex number z	$\lvert z\rvert$
argument of complex number z	arg z
vector of magnitude A	$\mathbf{A}$
scalar product of **A** and **B**	$\mathbf{A} . \mathbf{B}$
vector product of **A** and **B**	$\mathbf{A} \times \mathbf{B}$, $\mathbf{A} \wedge \mathbf{B}$
nabla or del, $\left(\mathrm{i}\frac{\partial}{\partial x} + \mathrm{j}\frac{\partial}{\partial y} + \mathrm{k}\frac{\partial}{\partial z}\right)$	∇
Laplacian operator, $\left(\frac{\partial^2}{\partial x^2} + \frac{\partial^2}{\partial y^2} + \frac{\partial^2}{\partial z^2}\right)$	∇^2

• See note on use of d or *d*, p. 1681.

D. Abbreviations (Symbols) for the Names of Units

(Letters of the Latin alphabet used for this purpose are to be printed in roman type.)

1. *Internationally Accepted Units.*

(The use of small roman capitals for single capital letter abbreviations is permissible.)*

metre	m
micron	μ
ångström	Å
square metre	m^2 ... sq.m
cubic metre	m^3 ... cu.m
cubic centimetre †	cm^3 ... cu.cm ... c.c.
litre	l.
second	s ... sec
minute	min
hour	h
hertz	Hz
cycles per second	c/s
revolutions per minute	rev/min
gramme	g
kilogramme (mass)	kg
kilogramme (force)	Kg
dyne	dyn
newton	N
bar	b
atmosphere (pressure)	atm
poise	P
joule	J
watt	W
watt-hour	Wh
calorie	cal
kilocalorie	kcal
degree Celsius	°C
degree centigrade	°C
degree Fahrenheit	°F
degree Kelvin	°K
lumen	lm
lux	lx
stilb	sb
candella	cd
electrostatic unit	e.s.u.
electromagnetic unit	e.m.u.
Debye unit	D
coulomb	C
ampere	A ... amp
volt	V
ohm	Ω
electron-volt	eV
volt-coulomb	VC
volt-ampere	VA
farad	F
henry	H
gauss	G
weber	Wb
normal concentration	N
molar concentration	M
molal concentration	m
hydrogen-ion exponent	pH

2. *Prefixes to Abbreviations for the Names of Units indicating*

Multiples.		*Sub-multiples.*	
tera ($\times 10^{12}$)	T	deci ($\times 10^{-1}$)	d
giga ($\times 10^{9}$)	G	centi ($\times 10^{-2}$)	c
mega ($\times 10^{6}$)	M	milli ($\times 10^{-3}$)	m
kilo ($\times 10^{3}$)	k	micro ($\times 10^{-6}$)	μ
		nano ($\times 10^{-9}$)	n
		pico ($\times 10^{-12}$)	p

3. *Common British Units.*

inch	in.	ounce	oz.
foot	ft.	pound (mass)	lb.
yard	yd.	hundredweight	cwt.
square inch (similarly for foot, etc.)	$in.^2$, sq.in.	pound (force)	Lb.
cubic inch (similarly for foot, etc.)	$in.^3$, cu.in.	poundal	pdl.
		foot-pound	ft.Lb.
gallon	gal.	horse power	h.p.
grain	gr.	British thermal unit	B.Th.U.

* Small capital letters will be used in such cases in the Chemical Society's publications.

† c.c. (or its alternative ml.) will normally be used in the Chemical Society's publications.

E. Some Abbreviations for Words other than Names of Units

This list is not intended to be exhaustive. The words in this list will often be given in full in the text, but where abbreviations are used the following forms are recommended.

(*To be printed in roman type.*)

absolute	abs.
alternating current	a.c.
anhydrous	anhyd.
approximate (-ly)	approx., *ca.*
aqueous	aq.
atmospheric	atm.
atomic weight	at.wt.
boiling point	b.p.
calculated	calc.
centre of gravity	c.g.
coefficient	coeff.
compound	cpd.
concentrated	conc.
concentration	concn.
constant	const.
corrected	corr.
critical	crit.
crystalline, crystallized (adjective)	cryst.
current density	c.d.
decomposition	decomp.
degree	deg.
dilute	dil.
direct current	d.c.
distilled	dist.
electromotive force	e.m.f.
equation	eqn.
equivalent	equiv.
experiment (-al)	expt.
figure (diagram)	fig.
freezing point	f.p.
gram molecule	mole
horse power, brake	b.h.p.
horse power, effective	e.h.p.
horse power, indicated	i.h.p.
horse power, nominal	n.h.p.
horse power, shaft	s.h.p.
infra-red	i.r.
insoluble	insol.
latent heat	lat.ht.
liquid	liq.
magnetomotive force	m.m.f.
maximum	max.
melting point	m.p.
minimum	min.
molecule, molecular	mol.
molecular weight	mol.wt.
observed	obs.
per cent	% (or in full)
potential difference	p.d.
precipitate	ppt.
preparation	prep.
recrystallized	recryst.
relative humidity	r.h.
root mean square	r.m.s.
section, paragraph	§
soluble	sol.
solution	soln.
specific	sp.
specific gravity	sp.gr.
specific heat	sp.ht.
specific volume	sp.vol.
standard temperature and pressure	s.t.p.
temperature	temp.
ultra-violet	u.v.
vacuum	vac.
vapour density	v.d.
vapour pressure	v.p.
volume	vol.
weight	wt.

ALPHABETICAL INDEX

OF recommended symbols for physical quantities including single letters denoting mathematical constants and operations but not single-letter abbreviations for names of units or other words.

(*Names of independent quantities are separated by colons; alternative names for a single quantity are separated by semicolons. Enclosure of the name of a quantity in parentheses indicates that there is an alternative symbol of equal standing; enclosure in square brackets indicates that there is another symbol which is preferred. An asterisk against the name of a quantity indicates that the specified symbol is always used with a subscript when denoting that quantity.*)

A	area : atomic weight
$\mathbf{A}$, A	magnetic vector potential
a	acceleration : activity, relative
B	(luminance; brightness) : susceptance
$\mathbf{B}$, B	magnetic flux density; magnetic induction
b	breadth
C	heat capacity per mole : (concentration) : capacitance
c	heat capacity per unit mass : (concentration)
$\mathbf{c}$, c	speed of light
D	differential operator
D	diffusion coefficient
$\mathbf{D}$, D	electric flux density; electric displacement
d	differentiation
∂	partial differentiation
d	diameter : relative density : current density at an electrode surface
E	(energy) : Young's modulus : activation energy : illumination : electromotive force : single electrode potential *
$\mathbf{E}$, E	electric force; electric field strength
e	base of natural logarithms
$-\mathbf{e}$, $-e$	charge of electron
F	force : free energy; Helmholtz function : (luminous flux)
$\mathbf{F}$, F	Faraday's constant
f	(frequency) : [acceleration] : (activity coefficient)
G	rigidity : Gibbs function : conductance
$\mathbf{G}$, G	gravitational constant
g	gravitational acceleration : osmotic coefficient
$\mathbf{g}$, g_0	gravitational acceleration, standard value
H	heat function; enthalpy; total heat
$\mathbf{H}$, H	magnetic field strength; magnetizing force
h	height
$\mathbf{h}$, h	Planck's constant
$\mathbf{I}$, I	[intensity of magnetization]
I	moment of inertia : luminous intensity : electric current : ionic strength
i	(square root of minus one)
$\mathbf{J}$, J	current density
j	(square root of minus one)

K	bulk modulus : equilibrium constant of chemical reaction
k	radius of gyration : (thermal conductivity) : velocity constant of chemical reaction
$\boldsymbol{k}$, k	Boltzmann's constant
L	(luminance; brightness) : inductance, especially self-inductance : inductance, self or mutual *
l	length : [equivalent ionic conductance *]
$\mathbf{M}$, M	(intensity of magnetization)
M	moment : bending moment : molecular weight : mutual inductance
m	mass : molality
$\boldsymbol{m}$, m	mass of electron
N	number of molecules
$\boldsymbol{N}$, N	Avogadro's number
n	number of moles : refractive index *
P	(pressure) : power
p	(pressure)
Q	(quantity of heat) : electric charge : power, reactive : partition function
q	(quantity of heat)
R	luminous radiance : resistance
$\boldsymbol{R}$, R	gas constant per mole : Rydberg's constant
r	radius : spherical or cylindrical coordinate : (resistivity; specific resistance)
S	entropy : power, apparent
$\mathbf{S}$, S	Poynting vector
T	period : kinetic energy : torque : temperature, absolute : (transport number *)
t	time : [temperature, empirical] : (transport number *)
U	internal energy
u	(velocity)
V	(volume) : potential energy : potential : potential difference : (electromotive force)
v	(volume) : (velocity)
W	weight : (work) : (energy) : energy, electrical
w	(work) : weight fraction
X	reactance
x	coordinate : mole fraction
Y	admittance
y	coordinate
Z	modulus of section : atomic number : impedance
z	coordinate : valency of an ion
α	(angle) : angular acceleration : coefficient of thermal expansion : degree of dissociation : light absorption factor
β	(angle) : luminance factor
$\boldsymbol{\beta}$, β	Bohr's magneton
Γ	surface concentration
γ	(surface tension) : ratio of specific heats : (activity coefficient, especially stoichiometric) : (conductivity; specific conductance)
Δ	increment or finite difference operator
δ	increment or finite difference operators : dielectric loss angle
ϵ	[base of natural logarithms] : permittivity
ζ	electrokinetic potential
η	efficiency : viscosity : electrolytic polarization; overpotential
θ	(angle) : spherical coordinate : temperature, empirical
κ	compressibility : magnetic susceptibility, volume : conductivity; specific conductance, especially of electrolytes
Λ	equivalent conductance : equivalent ionic conductance *

λ	wave-length : (thermal conductivity) : activity, absolute
μ	coefficient of friction : Joule–Thomson coefficient : chemical potential : [refractive index *] : permeability : dipole moment
ν	(frequency) : (wave number) : [Poisson's ratio] : kinematic viscosity : stoichiometric number of molecules
$\tilde{\nu}$	(wave number)
Π	product
$\varPi$	osmotic pressure
π	ratio of circumference to diameter
ρ	density : light reflexion factor : electric charge density, volume : (resistivity; specific resistance)
Σ	summation
σ	Poisson's ratio : (surface tension) : electric charge density, surface : (conductivity; specific conductance)
σ, σ	Stefan–Boltzmann constant
τ	light transmission factor
$\varPhi$	(luminous flux) : magnetic flux
ϕ	(angle) : spherical or cylindrical coordinate : fluidity : electronic exit work function : phase difference : volume fraction
χ	magnetic susceptibility, mass
$\varPsi$	electric flux
ψ	(angle)
ω	solid angle : angular velocity

PROCEEDINGS

OF THE

CHEMICAL SOCIETY

Minutes of a

SCIENTIFIC MEETING

held at Burlington House on May 3rd, 1951, at 7.30 p.m.

PROFESSOR W. WARDLAW, C.B.E., D.Sc., Vice-President, was in the Chair, and welcomed Professor H. Dingle, President of the Royal Astronomical Society, and the Fellows of that Society and of the Geological Society, who were invited to the Meeting.

MINUTES.

The Minutes of the Scientific Meeting held at Burlington House on April 26th, 1951, were read, and were confirmed and signed.

FORMAL ADMISSION OF FELLOWS.

The following were admitted Fellows of the Society: C. H. Thomas, T. P. McLaughlin, C. N. Hunter, J. M. Thorp, Y. Pocker, L. T. Dowling.

LECTURE.

After a brief introduction the Chairman called upon Professor H. C. Urey to deliver the lecture entitled "Chemical Evidence relative to the Origins of the Earth and Planets."

At the conclusion of the lecture, a vote of thanks to Professor Urey, proposed by Professor Dingle, was carried with acclamation.

Minutes of a

SCIENTIFIC MEETING

held in the Lecture Theatre of The Royal Institution on May 10th, 1951, at 7.30 p.m.

The President, PROFESSOR E. K. RIDEAL, M.B.E., M.A., D.Sc., F.R.S., was in the Chair, and welcomed Dr. Mata Prasad (Bombay) and Professor H. C. Urey (Chicago), who were present.

MINUTES.

The Minutes of the Scientific Meeting held at Burlington House on May 3rd, 1951, were read, and were confirmed and signed.

FORMAL ADMISSION OF FELLOWS.

The following were admitted Fellows of the Society: J. R. Millar, C. D. Kopkin, D. N. Kirk, A. J. Groszek, J. Chanmugam, E. D. M. Dean.

LIVERSIDGE LECTURE.

After a brief introduction, the President called upon Professor H. W. Melville, F.R.S., to deliver the Liversidge Lecture entitled "Transient Entities in Chemical Reactions."

At the conclusion of the Lecture, a vote of thanks to Professor Melville, moved from the Chair, was carried with acclamation.

OFFICIAL ANNOUNCEMENTS

DEATHS.

The Council regret to announce the deaths of the following Fellows :

	Elected.	Died.
Richard Westman Challinor (Sydney) ...	Dec. 5th, 1912.	Feb. 3rd, 1951.
Eric Morgan Hall (Hull).....	May 15th, 1941.	Feb. 6th, 1951.
Heinz Peter Koch (Manchester)	Sept. 7th, 1942.	Mar. 24th, 1951.
George Armand Robert Kon (S.W.3) (C. 1931—32, 1933—36).....	May 1st, 1919.	Mar. 15th, 1951.
Joseph Henry Lane (Taplow)	Nov. 20th, 1941.	Mar. 9th, 1951.
Richard William Merriman (E.10).....	June 15th, 1911.	Dec. 29th, 1950.
Henry Richard Napp (W.C.2)	Feb. 21st, 1929.	Mar. 26th, 1950.
Frederic William Richardson (Bournemouth)	Feb. 1st, 1883.	Dec. 17th, 1950.
Emil Alphonse Werner (Dublin)	Feb. 18th, 1888.	Mar. 18th, 1951.
John Pierce Wilson (Oxford).....	Mar. 7th, 1946.	Mar. 31st, 1951.

CONGRATULATIONS.

(a) 60 *years of Fellowship.*

The President has conveyed the congratulations of the Society to Dr. Gilbert John Fowler (Bangalore), who completed 60 years of Fellowship on May 7th, 1951.

(b) 50 *years of Fellowship.*

Congratulations have also been conveyed to the following, who completed 50 years of Fellowship on May 2nd, 1951 :

Percival James Burgess (Church Crookham).
Ernest Clark (Highcliffe).
Eustace Coddington (Leatherhead).
Henry Drysdale Dakin (New York).
Albert Ernest Dunstan (Cambridge).
John Vargas Eyre (Epsom).
Lord Henley (Rugby).
Alexander McKenzie (Dundee).
Charles Edward Kenneth Mees (Rochester, New York).
Edgar David Maurice Neumann (Barking).
William Henry Taylor (Cobham).

ELECTION OF NEW FELLOWS.

The following 171 candidates were elected Fellows of the Society on May 10th, 1951 :

Rudolph Abraham Haim Abramovitch.
John Lynde Anderson.
Robert Craig Anderson.
Charles Leslie Angyal.
Kurt Robert Simon Ascher.
Frank Peter Avonda.
Herbert Josiah Bache.
Guy Houghton Baker.
Edgar John Barnard.
Arthur John Beckwith.
Muus Gerrit Jan Beets.
Ronald Frederick Bird.
Alexander Blackhall.
Edward Bloom.
Kenneth Bolsover.
Norman Boulter.
John Edward Llewellyn Bowcott.
Freda Bowyer.
Erwin Brand.
Joseph Clair Brown.
William Orr Brown.
Joseph Lindsay Bryson.
Charles Merlyn Buess.
Harold Halsall Burns.
Gerald Charles Bye.
John Ivan George Cadogan.
Brian Capon.
Kenneth Roy Capper.
Richard Jeremy Lorains Carter.
Albert Cecil Case.
Stanley Arthur Clarke.
Alan John Cleaver.
Robert Lynn Cole.
Harold John Collins.
Anthony Morris Cottrell.
Roland Edwin Coulson.
Edward Basil Craddock.
Allan Crawshaw.
Albert Gruffydd Davies.
Arthur Leslie Davis.
Rolf Dessauer.
Jean Pierre de Villiers.
Edwin Dorfman.
Leonard Andrew Duncanson.
Alexander Simpson Dunn.
Jerome Fields Eastham.
Ernest Ludwig Eliel.
David John Elliott.

Horst Elsner.
Mario R. Falco.
Cyril Herbert Fawcett.
Henry Feuer.
William Crompton Firth.
Norman William Fletcher.
Brian Duncan Flockhart.
John Lambert Forryan.
Robert Wagner Freedman.
Robert McNaught Gailey.
Emery Martin Gal.
Brian Conrad Gardner.
Donald James Goodwin.
Bernard Clyde Paulin Goss.
Norman Greenhalgh.
Herbert Isaac Hadler.
Oscar Hagger.
Emil Amitai Halevi.
James Henry Halliday.
Norman Colin Harris.
Thomas Drysdale Heyes.
Eric Francis Hockings.
Michael Horsman.
John Denis Arthur Hutchings.
Harold Leonard Jackson.
Gert Jacobowitz.
Alfred Jay.
Harold Douglas Jefferies.
Alan Johnson.
Francis Patrick Johnson.
Kenneth George Johnson.
Maurice Frederick Anthony Jones.
John Nelson Judy.
Alan William Jukes.
Alex Ervin Kelley.
William Palmer Kemp.
Richard Wightman Kierstead.
Harold Goodwin Cecil King.
Donald Monroe Kirschenbaum.
Harold Kwart.
John Andrew Lamberton.
Alfred John Legge.
Daniel Letteron.
Ralph Manuel Levine.
Yu-Cheng Liu.
John West Loder.
Edward Thomas Losin.
Peter McDonald.
Deryk Leonard Maker.
Harold Markowitz.
Raymond Leslie Martin.
Douglas Harry Mathews.
Everett William Maynert.
Arnold Mendelowitz.
Ralph Edward Miegel.
John Thomas Mills.
Peter William Drake Mitchell.
Frank Joseph Modic.
Raymond Frederick Moore.
William Henry Dunne Morgan.
Donald Frank Charles Morris.
Max Mousseron.
Maurice Francis Robinson Mulcahy.
Walter Thomas Longcroft Neal.
Alex Nickon.
Cecil Wilfred Nutt.
Geoffrey Osgood.
Eric Richard Osler.
Walter Simpson Owen.
John Colin Parker.
Robert Pascoe.
Leonard Pearson.
Shirley William Pelletier.
Donald Roy Penny.
Regina Presser.
Robert Frank Prier.
Charles Wayne Rees.
John Stanley Roberts.
Alex Roebuck.
William Horace Rogers.
John Malcolm Ross.
Walter Alan Ross.
Ernst Max von Rudloff.
Joseph Henry Ruzicka.
Elhanafy Ahmed Sadek.
Edith Salzmann.
William Andrew Sandilands.
Rex Arthur Saunders.
Charles Timothy Savin.
Scott Searles, jun.
Wolfgang Manfred Schubert.
Bernard Leslie Shaw.
David Stanley Smith.
Dennis Clifford Smith.
Thomas Alfred Smith.
Ram Saran Srivastava.
Brian Stevens.
Marcus Andrew Stevens.
Raymond John Stone.
Frederick John Stubbs.
Robert Denison Stubbs.
Joyce May Swan.
Alan James Swinnerton.
Gordon Malcolm Tener.
Donald Robert Terrey.
Robert Howard Garry Thomson.
Arthur Ian Tiffin.
Ram Das Tiwari.
Joyce Toothill.
Ralph Charles Tutton.
Jean Mary Tyler.
Henricus Georgius Peter van der Voort.
George Vaughan.
James Veitch.
Lawrence George Albert Ward.
John Hans Weisburger.
Mrs. Dorothy Stevens Wescott.
Mary Whittaker.
John Kendall Williams.
Robert Wilson.
John Alexander Winterburn.
Clare Barnes Wylam.
Stefan Zajac.

JOURNAL OF THE CHEMICAL SOCIETY—FORMAT.

The Council have approved a recommendation to revert to the pre-war style of type in the *Journal* as from January, 1952, and to use a slightly thinner grade of paper than at present.

SCIENTIFIC MEETINGS 1951–52.

The following dates for Scientific Meetings during the Session 1951—52 have been approved by Council:

1951.	1952.
October 18th.	January 24th.
November 1st.	February 7th.
November 15th.	February 21st.
December 13th.	March 13th.
	March 27th.
	April 16th—18th Anniversary Meetings to be held in Dublin.
	May 8th.
	June 5th.

GIFTS.

Acknowledgment is made of gifts of the Society's publications from Mr. J. O. Crane, Sir Henry Dale, and Mr. E. M. Learmonth.

LIBRARY.

From July 16th until September 30th, 1951, the Library will be open from 10 a.m. to 5 p.m. daily, except during the fortnight August 6th to 18th inclusive, when it will be closed for revision and cleaning.

SYMBOLS, SIGNS, AND ABBREVIATIONS.

A Report by the Symbols Committee of the Royal Society (representing the Royal Society, the Chemical Society, the Faraday Society, and the Physical Society) has been prepared to supersede the Report issued in 1937 by the Joint Committee of the Chemical Society, the Faraday Society, and the Physical Society on "Symbols for Thermodynamical and Physico-Chemical Quantities and Conventions relating to their Use."

This Report, which is published in the *Journal* for June 1951, lists the Symbols, Signs, and Abbreviations recommended for British Scientific Publications and adopted for use forthwith in the *Journal*. Reprints are available from the Chemical Society, price 9*d*. per copy or 12*s*. per 25 copies (post free).

VAN 'T HOFF FUND.

The Committee of the Van't Hoff Fund for the endowment of investigations in the field of pure and applied chemistry invites applications for grants from the fund.

The amount available for 1952 is about 1250 Dutch guilders, and applications should be sent by registered post to "Het Bestuur der Koninklijke Nederlandse Academie voor Wetenscheppen, bestemd voor de Commissie van het 'Van't Hoff Fonds,' Trippenhuis, Kloveniersburgwal 29, Amsterdam," before November 1st, 1951. Applicants must state the amount of the grant desired and the purpose for which it is required.

MEETINGS OUTSIDE LONDON

LEEDS.

"The Use of Optically Active Compounds in the Study of Organic Reactions," by Dr. J. Kenyon, F.R.S.

A joint meeting with the University Chemical Society was held in the Department of Chemistry, The University, Leeds, on April 24th, 1951, with Professor F. Challenger in the Chair.

After briefly reviewing the evidence for acyl-oxygen fission in esters, the Lecturer described work on hydrogen phthalates, toluene-*p*-sulphinates and toluene-*p*-sulphonates of some optically active alcohols, in which alkyl-oxygen fission occurs. The resolved hydrogen phthalates of 1-phenylbut-3-en-1-ol are hydrolysed by 5N-alkali to yield the

optically pure alcohol; weak alkali gives racemic 4-phenylbut-2-en-2-ol. Similarly sodium (+)-phenyl-*p*-methoxyphenylmethyl phthalate gives the (+)-alcohol with alcoholic alkali, and the (±)-alcohol with aqueous alkali. The same compound with sodium toluene-*p*-sulphinate yields a racemic sulphone, while on storage it disproportionates to sodium phthalate and the normal ester, which has one esterifying group racemised. Ammonia gives an amine but no amide. Replacement of the –OMe group by –SMe does not affect these reactions, but replacement by $-SO_2Me$ prevents alkyl-oxygen fission.

After a discussion, a vote of thanks, proposed by Dr. J. W. Baker, was carried with acclamation.

NORTH WALES.

"Oxidation," by Professor M. G. Evans, D.Sc., F.R.S.

A joint meeting with the University College of North Wales Chemical Society was held in the Dobbie Lecture Theatre, Bangor, on May 3rd, 1951, with Mr. Glyn O. Phillips in the Chair.

Following a short discussion, Dr. A. C. Riddiford proposed, and Mr. David M. Jones seconded, a vote of thanks to the Lecturer which was accorded with acclamation.

LIST OF APPLICATIONS FOR FELLOWSHIP

(*Fellows wishing to lodge objection to the election of these candidates should communicate with the Honorary Secretaries within ten days of the date of publication of the* Journal *for June, 1951. Such objections will be treated as confidential. The forms of application are available in the Library.*)

Apellaniz, Joseph E. P., A.B. (Columbia). American. 112 W. 80th Street, New York City 24, New York, U.S.A. Student. *Signed by:* Bernard R. Bluestein, Michael A. Manganelli, J. F. Lane.

***Bovey, Doreen Mary,** B.Sc. and Ph.D. (Lond.). British. 12, Southern Road, East Finchley, N.2. Assistant Lecturer, University of Nottingham. *Signed by:* A. S. Anderson, John C. Roberts, J. A. Baker.

Bradbury, Mrs. Helena, B.Sc. and Ph.D. (Leeds), F.R.I.C. British. 15, Silverton Road, Aigburth, Liverpool, 17. Lecturer, College of Technology, Liverpool. *Signed by:* G. N. Copley, A. E. Findley, C. B. F. Rice.

Brown, William Burns, M.Sc. (Lond.), A.R.C.S., F.R.I.C. British. D.S.I.R., Pest Infestation Laboratory, London Road, Slough. Principal Scientific Officer. *Signed by:* F. P. Gloyns, H. J. T. Ellingham, E. I. Beeching.

***Burrill, Peter Martin.** British. 32, Hoodcote Gardens, Winchmore Hill, N. 21. Student, Northern Polytechnic, N.7. *Signed by:* W. Gerrard, I. L. Finar, W. A. Smeaton, C. G. Smith.

Carter, Albert Smith, M.S. and Ph.D. (Wisconsin). American. E. I. du Pont de Nemours & Co. Inc., Jackson Laboratory, P.O. Box 525, Wilmington 99, Delaware, U.S.A. General Assistant Director. *Signed by:* J. M. Tinker, W. S. Calcott, G. E. Holbrook.

***Cordner, John Pruen,** B.Sc. (Melbourne). Australian. Ashmead, Grimshaw Street, Greensborough, Victoria, Australia. Research Student. *Signed by:* N. V. Riggs, C. C. J. Culvenor, K. H. Pausacker.

Cotton, Joseph Bernard, A.R.I.C. British. 7, Maney Hill Road, Sutton Coldfield. Research Chemist, I.C.I. Ltd., Kynoch Works, Birmingham. *Signed by:* R. J. Doyle, J. C. Tatlow, M. Stacey, E. J. Bourne.

***Elphick, Oliver John.** British. BM/OJE, London, W.C.1. Student, Cambridge University. *Signed by:* C. Y. Almond, J. D. Bu'Lock, B. A. Thrush.

Ford, Raymond Eric. British. 21A, Chilwell Road, Beeston, Notts. Student, University of Nottingham. *Signed by:* D. O. Jordan, S. C. Wallwork, C. C. Addison.

***Harrisson, Raymond John.** British. 4, Wolseley Street, Drummoyne, N.S.W., Australia. Research Student, Sydney University. *Signed by:* R. J. W. Le Fèvre, T. Iredale, J. Cymerman.

Hudson, John, M.A. (Oxon). British. Sideways, Pretoria Road, High Wycombe, Bucks. Director of Research, Lintafelt Ltd. and Director, Chiltern Research Laboratories Ltd. *Signed by:* G. Lewi, E. F. MacTaggart, J. W. Barrett.

Johnson, Edward Alexandre, M.A. and D.Phil. (Oxon). British. 1, Fairmead Road, London, N.19. Research Chemist, M.R.C. Spectrographic Unit. *Signed by:* G. H. Beaven, W. J. Oldham, S. F. Birch.

Kenyon, Richard Lee, A.B. (Illinois), Ph.D. (N. Carolina). American. Bush House, Aldwych, W.C.2. Associate Editor, Industrial and Engineering Chemistry and Chemical Engineering News. *Signed by:* L. H. Lampitt, J. W. Bushill, C. A. Bassett.

***Langford, Richard David.** British. 21, Castle Avenue, Dover. Student, University College, Southampton. *Signed by:* K. R. Webb, E. Cartmell, A. R. Burkin.

*Levy, Aaron. British. 56, Wilbury Crescent, Hove. Student, Brighton Technical College. *Signed by:* D. B. Schaverien, N. H. Pratt, J. H. Waton.

Lonie, William, B.Sc. and Ph.D. (Edin.). British. British Rayon Research Association, Barton Dock Road, Urmston, Manchester. Research Chemist. *Signed by:* H. R. Cooper, J. Kenner, J. L. Bolland.

McCallum, John Rowan, B.Sc. (McGill). Canadian. 11, South Parade, Weston Point, Runcorn. Research Chemist, Peter Spence & Sons Ltd., Widnes. *Signed by:* S. Hill, T. Lenton Elliott, R. Sidlow.

*Macleod, Norman, A.R.C.S. British. 69, South Knighton Road, Leicester. Assistant Lecturer, University College, Leicester. *Signed by:* E. R. A. Peeling, L. Hunter, F. R. Shaw.

*Ogleby, John Wilson, B.Sc. (Dunelm). British. 9, Church Street, Durham City. Research Student. *Signed by:* F. A. Paneth, G. R. Martin, J. R. Richards.

*Peacock, Ernest Walter. British. 122, Union Road, Dover. Student, Southampton University College. *Signed by:* K. R. Webb, E. Cartmell, A. R. Burkin.

Ray, Richard Dennistoun, B.A. (Cantab.), A.R.I.C. British. c/o Farley's Infant Food Ltd., Torr Lane, Plymouth. Chemist. *Signed by:* H. T. S. Britton, S. J. Gregg, C. L. Silverstone.

*Seal, Kenneth Thomas. British. 48, Park End Road, Romford. Student. *Signed by:* H. Holness, R. A. Tingey, G. Mattock.

Shiner, Vernon Jack, jun., Ph.D. (Cornell). American. 8, Castleton Avenue, Wembley. Research Fellow. *Signed by:* Kathleen M. Jackson, E. D. Hughes, C. K. Ingold.

*Stanley, Paul Crosby, B.Sc. (Lond.). British. 67, Broxholm Road, West Norwood, S.E.27. National Service. *Signed by:* A. J. Warwick, W. A. Swindin, A. Alsbury, J. A. Baker.

Tiedt, Johannes, M.Sc. (South Africa). South African. Department of Textile Industries, The University, Leeds, 2. Research Assistant. *Signed by:* A. B. Meggy, E. V. Truter, C. S. Whewell.

*Turpin, Derek George, B.Sc. (Lond.), M.A. (Emory Univ.). British. 170, Lakedale Road, Plumstead, S.E.18. Research Student, King's College, London. *Signed by:* D. H. Hey, R. A. Heacock, R. D. Mulley.

*Wait, Eric. British. Balliol College, Oxford. Student. *Signed by:* R. P. Bell, H. M. Powell, W. A. Waters.

*Whittaker, Kenneth. British. 26, Ton Glas, Bryntirion, Nr. Bridgend. Assistant Chemist to Fine Dyestuffs & Chemicals Ltd., Bridgend. *Signed by:* D. P. Evans, Leo Ivanovsky, J. W. Batty.

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PAPERS RECEIVED.

(List of papers received between April 20th and May 18th, 1951.)

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"The effect of *tert.*-butyl substituents on the formation of indanthrone and flavanthrone from 2-aminoanthraquinone. The mode of formation of flavanthrone in the alkali fusion of 2-aminoanthraquinone." By W. Bradley and H. E. Nursten.

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"Experiments on the synthesis of the pyrethrins. Part VI. New syntheses of the cinerolones." By L. Crombie, S. H. Harper, R. E. Stedman, and D. Thompson.

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"Studies of solutions of alcohols in non-polar solvents. Part I. The solubility and heat of solution of water in dilute solutions of alcohols in benzene." By L. A. K. Staveley, R. G. S. Johns, and B. C. Moore.

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"Cordycepin. A metabolic product from cultures of *Cordyceps militaris* (Linn.) Link. Part I. Isolation and characterisation." By K. G. CUNNINGHAM, S. A. HUTCHINSON, W. MANSON, and F. S. SPRING.

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